"I would have everie man write what he knowes and no more."—MONTAIGNE

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EDITORIAL

CLAUDE BERNARD in his *Leçons sur les phénomènes de la vie* drew the conclusion that " All the vital mechanisms, varied as they are, have only one object, that of preserving constant the conditions of life in the internal environment." Prof. J. S. Haldane comments on that as follows: "No more pregnant sentence was ever framed by a physiologist." It is obvious that all life, all physiological activity, tends to alter, to modify by this activity, the conditions of life in the internal environment and it is only by the action of these vital mechanisms which come into play immediately and with the necessary vigour that the condition of the internal environment is kept constant. How sensitive is the mechanism which maintains this constancy may be judged from the fact that a 0.23 per cent increase in the CO_2 content of the alveoli will increase breathing 100 per cent.

In the July number and again in this one Dr. A. B. Dobkin tells us what complicated arrangements he and his colleagues have had to make to follow the changes which take place in the internal environment when such major operations are undertaken as cholecystectomies, lobectomies, pnemonectomies, etc. He recognizes that " No mechanical respirator presently available satisfies the varying requirements of the individual patient ", but believes that the " Educated hand " of the skilled anaesthetist can do something to remedy the deficiency of the machine. He points out, however, that in one case, in spite of the machine and the " Educated hand ", there was a significant fall in the pH while the pleura was open, but adds, " This corrected itself as the operation progressed "; so the vital mechanisms were evidently still active, reinforcing the efforts of the machine and the "Educated hand ", by the nice adjustments of which alone the vital mechanisms are capable. Injury has to be devastating or surgery drastic, to render them incapable of playing their accustomed role.

Brit. J. Anaesth. (1956), **28**, 344

ACUTE TOLERANCE TO THIOPENTONE IN MAN

BY

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ONE of us (J.W.D.) noted that although much smaller doses of thiopentone were given to patients at the Hospital of the University of Pennsylvania than at most centres in the British Isles, recovery of consciousness appeared to be equally prompt in all cases. To test the accuracy of this observation anaesthesia records from various hospitals in Liverpool were compared with those of the Philadelphia institution.

CLINICAL DATA

The anaesthesia technique compared was the intermittent administration of thiopentone, combined with nitrous oxide-oxygen, using the semi-open circuit at flow ratios of 4.5 : 1.5 or 6 : 2 litres per minute. No cases were included who received a volatile anaesthetic agent, a muscle relaxant or an intravenously administered analgesic. Records dealing only with surface operations were selected. The minimum duration of the procedures was 70 minutes, so that dosage figures for at least one hour of surgical anaesthesia were available for analysis.

Selection of cases was limited to patients of good physical condition under the age of 55 and suffering from no pathological condition other than that which necessitated the operation. The premedication consisted of 10 mg (1/6 grain) morphine for all patients combined with either 0.6 mg (1/100 grain) atropine or 0.4 mg (1/150 grain) scopolamine. Approximately one-third of the administrations in each country were by consultant anaesthetists, the remainder being given by residents or registrars with varying degrees of experience.

Table I gives details of the patients from each centre. The average total amount of thiopentone administered at 15-minute intervals is shown in figure 1. Irrespective of whether the actual dose in mg or the dose expressed in mg/kg is compared the British patients received approximately twice as much thiobarbiturate as the Americans for any given duration of anaesthesia. The average 30-minute requirements are significantly different by recognized statistical tests ($p<0.01$).

The possibility of factors peculiar to to the two different hospital groups being involved in this difference in requirements of thiopentone was excluded bv a small series of 27 cases anaesthetized at the Hospital of the University of Pennsylvania with double its average induction dose (7.84 mg/kg thiopentone). The average total amount of thiopentone administered to these patients at the end of 30 minutes of anaesthesia was 14.9 mg/kg, which

TABLE I

Details of patients and nature of operations in a series of cases from America and Britain in whom thiopentone requirements were studied, together with the average induction and 30-minute dosage of the drug in each series.

Series	Hospital of the University of Pennsylvania	United Liverpool Hospitals
Number of cases	120	100
Average age (years)	40.0	44.8
Average weight (kg)	60.1	60.0
Nature of operations: for varicose veins	96	72
for plastic surgery	24	28
Average induction dose of thiopentone	212 mg 2.5 mg/kg	500 mg 8.3 mg/kg
Average dose administered at end of 30 minutes ...	411 ± 10.8 mg 7.0 ± 0.18 mg/kg	905 ± 22.0 mg 15.1 ± 0.13 mg/kg

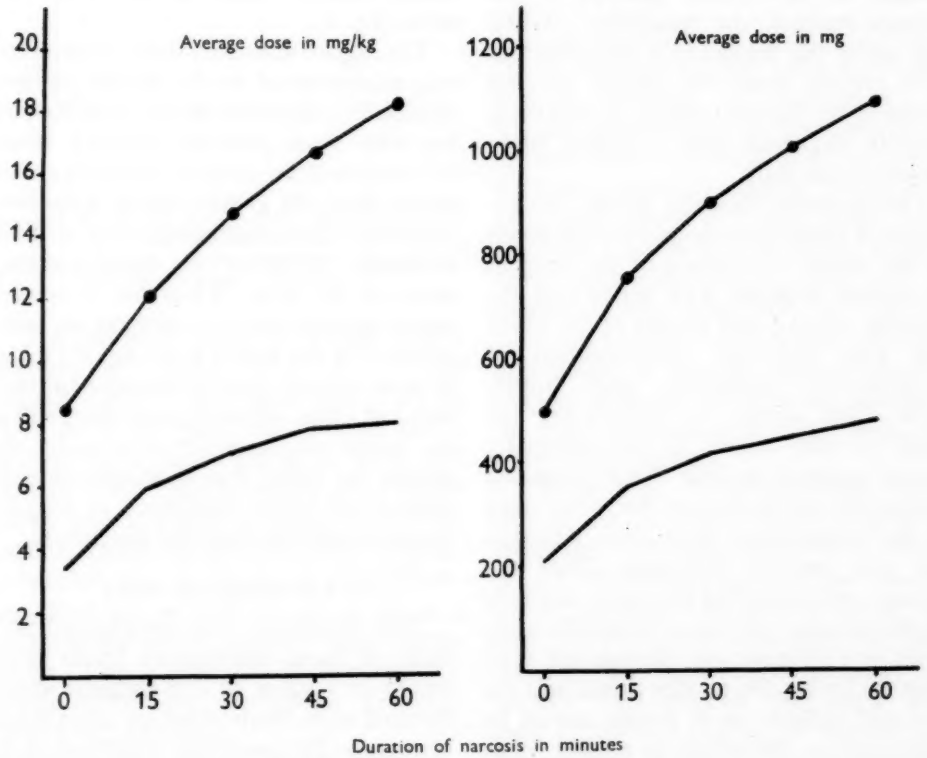

FIG. 1

Comparison of the average doses of thiopentone required during anaesthesia in two series of patients referred to in the text.

——— Hospital of the University of Pennsylvania.

●——● United Liverpool Hospitals.

compares closely with the figures (15.1 mg/kg) for the British patients. Conversely, Dundee (1955a) has described 21 patients, anaesthetized in Britain in whom the initial and 30-minute requirements of thiopentone were similar to those used in the Philadelphia hospital (2.4 and 4.6 mg/kg respectively). The awakening time for both groups was the same.

DISCUSSION

Since the return of consciousness was thought to be equally prompt in all patients studied, the possibility existed that either the thiopentone was removed more rapidly from the central nervous system in the British patients or that these subjects awakened with a higher brain content of the drug.

The pharmacologically active concentration of thiopentone in the blood depends on the degree of binding of the drug to the plasma proteins. This varies with the albumin content and the pH of the blood and also with the concentration of thiopentone (Goldbaum and Smith, 1954). The former two factors are unlikely to vary widely in the essentially normal patients studied. With increasing barbiturate concentration the percentage of the bound drug diminishes, although the total amount increases. Thus the patients who received the large amounts of thiopentone will have proportionately more free drug per mg/kg injected than those receiving the smaller doses, and the observed differences in dosage cannot be explained by differences in plasma binding.

In 1952 Brodie showed that the plasma concentrations at the time of orientation following small total doses of thiopentone were lower than the corresponding levels following larger total doses. The amounts of thiopentone given by Brodie (22–65 mg/kg) were well above those used in clinical anaesthesia, but if his findings apply with total doses varying from 5 to 18 mg/kg, they would throw light on why the return of consciousness in the British patients was as prompt as in those anaesthetized in the United States. However, they do not explain why the increment doses required in the British series of cases was approximately double those of the American series (fig. 1).

The higher induction doses of thiopentone administered to the British patients may be the important factor in determining why these patients required larger increments of the drug to maintain anaesthesia, since the greater initial brain concentration of thiobarbiturate may result in increased tolerance to supplementary doses of the drug. When the increment doses required every 15 minutes are compared with the initial dose (fig. 2), it can be seen that the ratio is the same for both series of cases. This suggests that, within the range of dosage of this study, the greater the initial dose of thiopentone the greater will be the increments of drug required to maintain surgical anaesthesia.

EXPERIMENTAL DATA

This hypothesis was investigated by a study of blood thiopentone levels at recovery in a series of 119 patients anaesthetized with single doses or intermittent injections of thiopentone, combined in the latter case with nitrous oxide-oxygen. Atropine 0.4–0.6 mg (1/150–1/100 grain) was the only drug given prior to anaesthesia.

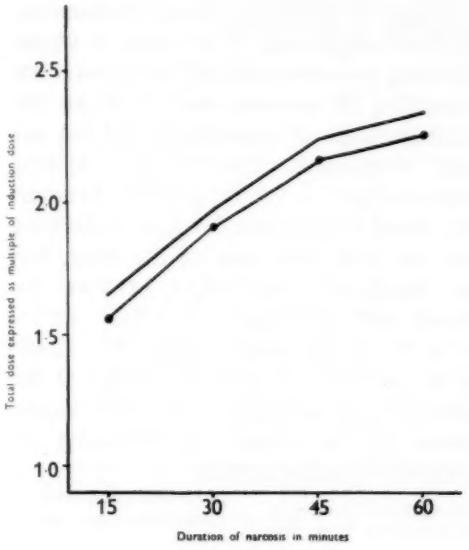

FIG. 2

Comparison of ratio of total dose of thiopentone required during anaesthesia to the induction dose in same series of patients.
——— Hospital of the University of Pennsylvania.
●——● United Liverpool Hospitals.

The subjects were fit female adults within the weight range of 110–160 pounds (50–73 kg), with ages varying from 16 to 44 years. All patients had a pre-operative haemoglobin of 11 g per cent or over. The operations were either minor gynaecological procedures or body surface operations such as plastic surgery. It was felt that the degree of pain following these was so little as not to act as a stimulus and hasten recovery from anaesthesia. The occurrence of hypotension, severe blood loss, or hypoxia excluded cases from this study.

The exact moment of return to consciousness is difficult to define and in the early cases several endpoints were used. From these the moment when the patient would open her eyes in response to a command was selected as being the most reliable. Blood was drawn slowly over a period of 30 to 60 seconds so that the average blood thiopentone level for the period immediately following the return of consciousness could be determined. In order to be certain that the patients were awakening from the effects of thiopentone and not because of elimination of nitrous oxide no patient was included in whom the desired endpoint was elicited within five minutes of withdrawal of the inhalation agent.

It has been shown by Price and Conner (1956) that two minutes after rapid intravenous injection of thiopentone the brachial arterial and jugular venous blood levels of the drug differ little and thereafter decline in a parallel manner. This does not necessarily apply to venous blood drawn from the forearm or anticubital fossa, as some thiopentone may diffuse into the muscles and fat of the limb. In an attempt to obtain samples which would give readings similar to those of jugular venous or arterial blood the veins on the dorsum of the hand or around the wrist were used whenever possible.

Thiopentone determinations were carried out on whole heparinized blood using the technique described by Brodie et al. (1950) for plasma. Where possible several samples were drawn before and after recovery from anaesthesia and these revealed that the decline in blood barbiturate concentration was rarely more than 1 mg/litre during the period from five minutes before to five minutes after the return of consciousness. Thus, if the assessment of the endpoint was not accurate, the degree of error was not gross.

Figure 3 shows the blood levels at awakening in 15 patients who received varying single doses of thiopentone. There is a significant ($p<0.01$) relationship between the dosage and the blood thiopentone level at recovery (correlation coefficient (r) $= +0.74$).

Thus Brodie's observations are applicable for single injections of thiopentone within the range of dosage used in clinical anaesthesia. However, these findings do not indicate whether the initial dose of the drug, the total dose, or the duration of anaesthesia is the important factor in determining the blood level of thiopentone at which consciousness will return following intermittent injections of this substance.

Figure 4 shows the blood thiopentone levels at awakening in 72 cases, to whom the drug was administered for periods not exceeding 20 minutes and in whom the total duration of anaesthesia did not exceed 40 minutes. This reveals a striking relationship ($r = +0.88$; $p<0.01$) between the blood thiopentone level at awakening and the induction dose of the drug, and no significant relationship between the blood level and total ($r = +0.20$; $0.05<p<0.10$) or increment doses ($r = -0.06$; $0.50<p<0.60$). Within the limits of the duration of administration and anaesthesia set out above, the following regression equation applies:

$$\text{Blood thiopentone level at awakening in mg/litre} = 1.88 \times (\text{induction dose of thiopentone in mg/kg}) + 0.45.$$

FIG. 3
Blood thiopentone levels at awakening in 15 patients who received single injections of the drug.

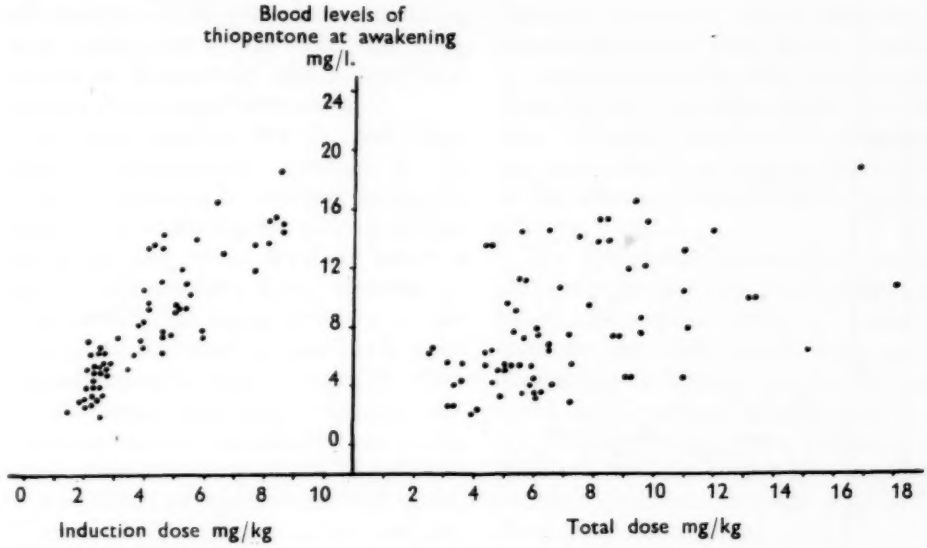

FIG. 4

Relationship between the blood thiopentone levels at awakening and the induction and total doses of the drug in 72 patients who were anaesthetized by intermittent injection of thiopentone. In these subjects the duration of administration did not exceed 20 minutes and the total period of unconsciousness was 40 minutes or less.

If the limitations of duration of anaesthesia and unconsciousness set out above were exceeded, it was found that the blood thiopentone level at awakening was dependent on both the initial ($r = +0.18$; $0.10 < p < 0.20$) and total ($r = +0.25$; $0.10 < p < 0.20$) doses of the drug, although the degree of correlation with either of of these factors was not great.

The part played by the total dose in determining the blood thiopentone levels at recovery was investigated in 58 patients. These received an initial dose varying only from 2.25 to 2.75 mg/kg, with a wide variation in the total amounts administered. No time limit was placed on the duration of the administration (1–58 minutes) or the total period of anaesthesia (2–105 minutes). The results, shown in figure 5, reveal that with total doses up to three times the induction dose the blood thiopentone level at recovery was fairly constant. Above this limit there was a gradual but inconsistent increase in the blood thiopentone levels at recovery from anaesthesia. Analysis of these data (table II) shows that, despite the wide scatter of readings, the increase in blood thiopentone levels at awakening is statistically significant.

In the patients receiving intermittent injections of thiopentone, no relationship could be found between the blood thiopentone levels at awakening and the duration of anaesthesia, although such a relationship did exist after a single injection of the drug.

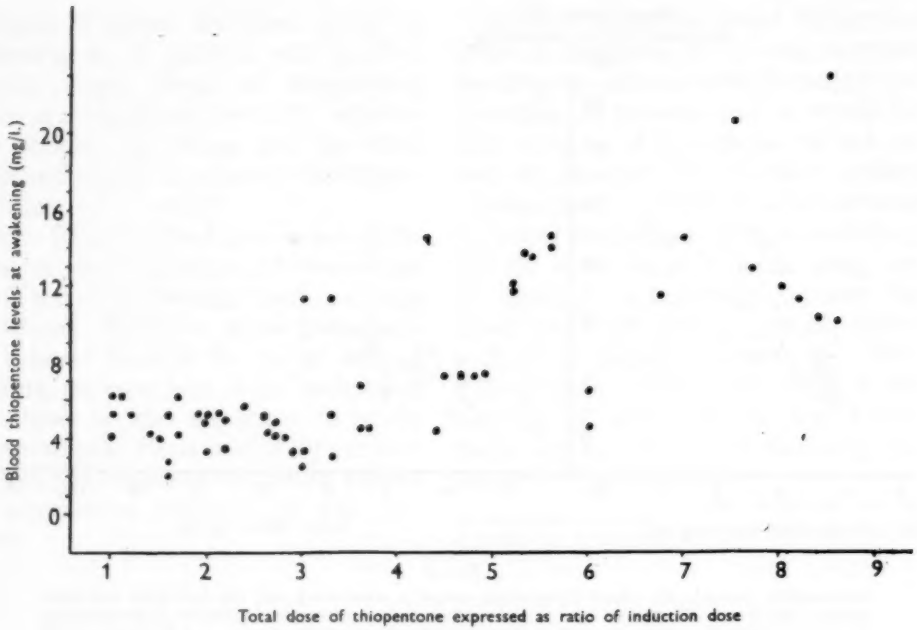

FIG. 5

Blood thiopentone levels at awakening in 58 subjects who received intermittent injections of thiopentone following an induction dose of 2.25–2.75 mg/kg related to the total dose administered (expressed as a ratio of the induction dose).

TABLE II

Analysis of blood levels of thiopentone on return of consciousness, related to total dose administered in patients receiving a constant induction dose of 2.25–2.75 mg/kg. Using "students" t test, each of the above average blood levels differs significantly from the others, the values for t being A-B 14.9, A-C 7.2, B-C 3.2.

	Ratio of total dose to induction dose	Number of observations	Average blood level on recovery (mg/litre)
A	Under 3	30	4.73 ± 0.152
B	3–6	19	8.20 ± 0.330
C	Over 6	9	12.56 ± 2.253

DISCUSSION

These observations show that there is a wide variation in the blood thiopentone levels at which normal patients awake from the doses of the drug used in clinical anaesthesia. The blood thiopentone level thus is not a reliable guide to the depth of anaesthesia. Contrary to the view expressed by Harris (1951) the degree of anaesthetic depression does not depend on the concentration of thiopentone in the circulating blood.

Brodie (1952) has suggested that the response of the central nervous system to thiopentone appears to depend on either the peak concentration or on the time of exposure of the tissues to the drug. From our results one can state that, with total doses of thiopentone not exceeding three times the induction dose, this latter determines the blood level at which patients

will awaken. With total doses exceeding three times the initial dose, the total amount of thiopentone administered also seems to be an important factor.

Our data suggests that the peak thiopentone concentration reached in the brain, whether this be attained during the induction or maintenance of anaesthesia, determines the blood level at which a patient will awaken from anaesthesia. With small total doses (relative to the initial dose) this peak is most likely to be reached during the induction period, while with the larger total doses, this peak concentration may be exceeded by one of the late supplementary injections. The greater the magnitude of the incremental doses, the more likely is this to occur, and the scatter in blood levels in figure 5 may be due to the variation in the size of the supplementary doses.

With the intermittent administration of thiopentone the time of exposure of the nervous system to thiopentone is not a factor *per se*, in determining blood levels at awakening.

The phenomenon of adaptation of the central nervous system to the narcotic effects of thiopentone has been called "acute tolerance", a term first used by Schmidt and Livingstone (1933) to describe the effects of morphine on the circulation. In contrast to chronically acquired tolerance, acute tolerance appears to develop rapidly after a single dose of drug. This is shown in figure 1, by the higher increment doses required to maintain anaesthesia in subjects induced with a large dose of the drug. Brodie (1952) has stated that adaptation of the central nervous system to the narcotic effects of thiopentone is not persistent and may last for less than one week. Apart from the fact that subjects have been shown to awaken at approximately the same blood level on three or four occasions within one hour, after repeated injections of thiopentone, our study throws no light on the duration of the effects of acute tolerance to thiopentone.

The agreement between the results of the dosage studies and the observations on blood thiopentone levels at awakening show that an unnecessarily large amount of thiopentone appears to have been used in the British cases. Unfortunately, it was not possible to compare the effects of such doses on the cardiovascular, respiratory or other systems with those produced by the smaller doses in the American series. However, as with all anaesthetic agents, it would seem desirable to administer the smallest amount of drug necessary to produce satisfactory operating conditions. Price and Helrich (1955) have found a linear relationship between the percentage reduction of the functional efficiency of the dog heart-lung preparation and the concentration of thiopentone to which it is exposed. Large doses also have a deleterious effect on liver function, the degree of impairment being roughly proportional to the total amount of thiopentone administered (Dundee, 1955b). There is as yet no evidence to suggest that acute tolerance develops to the effects of thiopentone on structures other than the central nervous system.

For these reasons it is suggested that the induction of anaesthesia should be accomplished with smaller doses of thiopentone than are currently in use in many centres in Britain. The initial injection, which can be given slowly, should not be

more than that required to produce sleep. Supplementary doses during the maintenance of anaesthesia should be kept to a minimum, except where momentarily deep anaesthesia is required. By these means the maximum concentration of the drug in the brain will be kept low and since this appears to govern the blood thiopentone concentration at which patients awake from anaesthesia, the total requirements of the drug should be appreciably reduced.

SUMMARY AND CONCLUSIONS

An analysis of average doses of thiopentone used in combination with nitrous oxide-oxygen to produce surgical anaesthesia was carried out in comparable series of patients anaesthetized at the Hospital of the University of Pennsylvania and at various hospitals in Liverpool. It was found that, for any given period of anaesthesia, the British anaesthetists administered approximately twice as much thiopentone as their American counterparts. Recovery appeared to be equally prompt in each centre.

Irrespective of the initial dose of thiopentone, a constant relationship was found between the total dose and the initial dose of the drug at any given duration of anaesthesia. Within the dosage range used in clinical anaesthesia, a linear relationship was found to exist between the blood thiopentone level at which patients awaken from a single injection of the drug and the amount injected.

Where the total dose of thiopentone did not exceed three times the induction dose, there was a striking relationship between the latter and the blood thiopentone levels at which patients awaken from anaesthesia, but no correlation could be found between the blood thiopentone levels at awakening and the total dose of the drug. When this range of dosage is exceeded, the total dose also played a part in determining the blood thiopentone level at which patients recover.

The above findings can be reconciled by the hypothesis that acute tolerance to the depressant effects of thiopentone on the central nervous system develops rapidly, the degree of adaptation being proportional to the peak concentration of thiopentone in the brain, whether this occurs during the induction of anaesthesia or following a supplementary dose of the drug.

The clinical application of these findings are discussed.

ACKNOWLEDGMENT

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ANAESTHESIA WITH CONTROLLED POSITIVE AND NEGATIVE PRESSURE RESPIRATION

PART II: REVIEW OF CARDIORESPIRATORY FUNCTION AND ACID-BASE HOMEOSTASIS

BY

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(*Continued from page* 323)

IN clinical anaesthesia the incidence of respiratory acidosis when the pleural cavity has been invaded for pulmonary or cardiopulmonary surgery remains the most serious problem (Beecher, 1950; Gibbon, 1950; Taylor, 1950; Miller, 1950, 1952; Maier, 1951; Gabbard, 1952; Etsten, 1953; and others). This problem can become even more exaggerated by using multiple anaesthetic agents (Ellison et al., 1955). In the presence of an open pleura the provision of adequate pulmonary ventilation is a harassing problem to the anaesthetist, for no anaesthetic procedure ties the clinician so closely to the rebreathing bag of the anaesthesia machine (Gibbon et al., 1955; Dobkin et al., 1955). During nonthoracic operations, with the patient in the supine position, the arterial pH and pCO_2 are a close function of the total ventilation (Buckley et al., 1953; Carpenter et al., 1953). On the other hand, patients during intrathoracic operations apparently require a much larger minute volume of ventilation than under normal awake conditions, as deduced from data of Gabbard (1952), Stead (1953), Allbritten (1954), Martin (1955), and others.

This primary allegiance to the patient's pulmonary ventilation produces a serious threat to life if difficulty develops due to rapid blood loss, excessive tracheobronchial secretions, cardiovascular depression from intermittent positive pressure respiration or inability to inflate or deflate the lungs adequately. Numerous advantages have been suggested by those who advocate the use of a mechanical respirator to take over this very urgent task of the anaesthetist. By hyperventilating the patient mechanically, the efforts on the part of the anaesthetist to provide adequate alveolar ventilation are greatly spared. Hyperventilation will also assist in overcoming the respiratory impediments of surgical pneumothorax, of operative posture (lateral and prone), and of retractors and packs; in overcoming resistance in anaesthesia equipment (Orkin et al., 1954, 1956); and in coping with inadequate carbon dioxide absorbers (Lund et al., 1956).

Elam and Brown (1956) have shown clearly that if the carbon dioxide absorber is not completely efficient, an elevated level of carbon dioxide in the inspired gas

results. Then very high rates of pulmonary ventilation using controlled breathing cannot completely clear the alveolar carbon dioxide. Hence respiratory acidosis is inevitable. Comparing expired alveolar carbon dioxide levels with closed and semiclosed systems and using up to 10 and 15 litres of anaesthetic gases per minute inflow rates and assisted or controlled breathing, they found that even this pulmonary ventilation was not sufficient to prevent carbon dioxide accumulation in some patients. In our study, where fresh soda lime was employed for each operation, the elevations of carbon dioxide which we observed could always be explained by other technical factors (anaesthetic management) or physiological factors (surgical pneumothorax, lung disease and intrathoracic manipulation and incision of bronchi and large vessels). Hyperventilation of these patients certainly assisted in maintaining near-normal levels of carbon dioxide.

The primary effects of hyperventilation are quite harmless (Brown, 1953) and its use should not be deterred from by the occasional clinician who still holds to the "need" for carbon dioxide or its usefulness in clinical anaesthesia (Kemp, 1954). No case of the chronic hyperventilation syndrome (Lewis, 1954) has ever been reported following use of hyperventilation during anaesthesia.

When hyperventilation is mechanically provided with a balanced anaesthetic technique employing analgesic, hypnotic and relaxant drugs it has been said that the surgeon can work in a quieter operative field, skeletal muscle tone and reflex pain responses are reduced, capillary oozing and oxygen consumption seem to be reduced, the doses of hypnotic drugs (thiopentone) and relaxant drugs are reduced (Dundee, 1955) and post-anaesthetic complications such as nausea, vomiting and hypotension occur less frequently (Dobkin et al., 1955; Bjork et al., 1956). Moreover, many clinicians have observed that it is difficult to eliminate carbon dioxide effectively under ordinary positive pressure ventilation and to avoid severe acidosis when abnormal postures or the open thorax are necessary for the surgical operation.

Respiratory acidosis during such surgery is unquestionably harmful (Altschule and Sulzbach, 1947; Orton, 1952; Miller et al., 1952; Campbell et al., 1953; Wilson et al., 1954; Merriman, 1955; Spurrell, 1955; Dripps and Severinghaus, 1955). It predisposes to shock and troublesome reflexes; it increases the requirements for anaesthetic agents; and it delays post-operative recovery. Thus most of the arguments for mechanical respirators are undoubtedly valid.

On the other hand, in clinical anaesthesia, one major and indisputable advantage of attentive manual assistance or control of the patient's breathing during open chest operations is that the anaesthetist can provide the surgeon with almost ideal working conditions. By remaining in constant contact with the patient's cardiorespiratory status the anaesthetist may be of more immediate benefit to the patient under difficult surgical circumstances than by attempting to provide the above named advantages with controlled breathing from a mechanical respirator.

The open chest requires an acute sense of awareness by the ordinary senses on

the part of the anaesthetist: the slight changes of the shades of blood in the wound; the throbbing light and dark pink of the lung surface with each heart beat and with each inflation; the varying shades of skin colour; the warm, dry skin which may insidiously change to a moist cold and clammy surface; and the rhythmic soft blowing sound of gases moving back and forth through the rebreathing tube, which may gradually develop slight crepitations or suddenly reveal bubbling râles. These must all be felt by the anaesthetist. It is therefore essential that his eyes remain on the operating field to provide the major guide to the administration of rhythmic compression of the rebreathing bag.

In the writers' opinion, this type of management provides the anaesthetist with a closer awareness of momentary changes in the patient's total condition than the use of a mechanical respirator, which almost always invites distraction of the anaesthetist's attention from the operation. Only when satisfactory lung deflation is a troublesome problem is a mechanical respirator invaluable. This is particularly so in the patient with parenchymatous lung disease which has destroyed the elasticity of the lungs. For some of these patients a subatmospheric phase in the cycles of the mechanical respirator may assist in providing better pulmonary ventilation and aid in the clearing of carbon dioxide where other means have been unsuccessful.

In planning the assessment of a mechanical respirator three foremost points of controversy must be considered. *First* are the possible benefits to the patient, as discussed above. *Second* are the recommended essential requirements of a mechanical respirator. *Third* are the major objections which surgeons and anaesthetists may have against such a device.

No mechanical respirator presently available satisfies the varying requirements of the individual patient, whether the surgical procedure involves a patient with cardiac or respiratory dysfunction or whether operation in the peritoneal or pleural cavity is being done. The surgeon is frequently harassed because the respirator causes rhythmic bulging of the diaphragm when he is working in the upper abdomen, or because of the ballooning of the lung when he is attempting a difficult hilar dissection. When the patient is incompletely relaxed or curarized these movements may be quite jerky. The anaesthetist is frequently harassed by the mechanical failings of the respirator, for in a moment of inattention he may miss a rapid development of overinflation, or a complete deflation of the reservoir. There is no signal to inform him that the relaxant drug has worn off until the surgeon complains of irregularities in respiration and jerky movements in the operative field.

Manually assisted or controlled respiration helps the skilled anaesthetist to provide the required amount of relaxant, analgesic and hypnotic drugs which will maintain smoothly the desired level of anaesthesia ("the educated hand"). The respirator removes this fine method of adjustment to individual "needs." The exhaustion of the Hering Breuer reflex or removal of some unknown visceral function of the lung producing a state of prolonged apnoea was less frequent and less

persistent until mechanical respirators came into use. This apnoea may be so intense that sometimes the patient is wide awake immediately postoperatively, but must be continuously ventilated or urged to breathe. It has been suggested that nikethamide is helpful in restarting spontaneous respiratory efforts in these cases (Wyant, 1953).

Even with the most efficient mechanical devices it sometimes requires continuous readjustment of the mechanics of the respirator, whether by a fixed volume or by a fixed pressure, to provide efficient pulmonary ventilation. It thus follows that the varying surgical and anaesthetic conditions in an individual patient together with the wide variety of ventilation requirements cannot be satisfied by a fixed setting on a mechanical respirator. When the control of respiration has been removed by relaxants, the machine does nothing to assist the anaesthetist in relating pulmonary ventilation to the metabolic requirements or metabolic derangements which may be developing. Only where prolonged respiratory paralysis exists can such aids as the Radford nomogram or arterial blood sampling for pH, pCO_2 and pO_2 determinations be of practical assistance (Whittenberger, 1955). Even at present the practical problems of measuring ventilation and alveolar carbon dioxide during anaesthesia require highly sensitive gas analysers and pressure recorders, whose interpretation must be carefully considered until simpler devices can be developed and tested (Elam et al., 1955; Eckenhoff et al., 1956).

Several anaesthetists have considered the essential requirements of a mechanical respirator (Musgrove, 1952; Mørch, 1954; Schultz et al., 1954; Pask, 1955a; Rollason, 1956). Of first importance is the need for a visible measure of the tidal volume which is delivered to the patient. This should be rapidly adjustable and reproduceable by the respirator. The inspiratory pressures must be variable up to a maximum of 30 mm Hg, which is controlled mechanically and released accurately at the desired peak pressure by an efficient blow-off valve. Inspiration and expiration together with a rest phase (expiratory pause) at atmospheric pressure should be variable so as to simulate the normal respiratory pattern, with an accelerating initial inflow followed by a quick release to atmospheric pressure on expiration (Cournand et al., 1952). When necessary, the use of subatmospheric pressure in the airway to assist the deflation of abnormal lungs should be sensitive enough to cut off when resistance to outflow has produced bronchiolar collapse.

The only possible indication for providing a lowered mean intrathoracic pressure during clinical anaesthesia (which would require a subatmospheric pressure phase) is in the patient with major cardiovascular disease who responds to intermittent positive pressure breathing with hypotension. This is most likely where an extensive abdominal operation is contemplated in a patient who is also suffering from a low circulating blood volume. Only when the lungs do not deflate well due to emphysema and fibrosis is the subatmospheric phase of value for intrathoracic operations. Surgical operations facilitated by abnormal postures on the operating table that may interfere with breathing or with the circulation may also be considered a relative indication for a low mean airway

pressure. With careful pre-operative preparation and continuous vigilance during the anaesthesia for such patients the real indication for a subatmospheric pressure phase in the breathing cycle should be uncommon (see figs. 11 and 12).

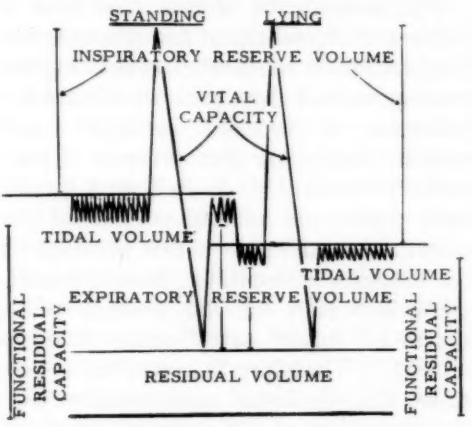

FIG. 11

Effect of posture on standard lung volumes and functional residual capacity (FRC).

The mechanical respirator should provide simple adjustments for producing a period of controlled lung inflation or breath-holding, and a small positive pressure at the end of expiration (if desired) for the occasional management of the last stages of chest closure (usually unnecessary); for expelling air from the pleural space; or for treating acute pulmonary oedema.

When spontaneous but shallow breathing is present while the pleura is closed, the respirator should be able to augment the volume of ventilation to the predetermined "normal needs" of the patient. This requires continuous control sensitivity on the respirator, just as manual assistance to respiration provides proper ventilation of the patient who is partially depressed. The mechanism of a respirator should be explosion-proof and not be wasteful of gases where the energy is derived from the respired gases or from compressed air. It is more important that each function of the respirator should have a separate mechanism which is easy to understand and to adjust than to have a machine which appears simple but in which a single mechanism performs several functions (Pask, 1955a).

In using a mechanical respirator, is it more important to provide a fixed minute volume of respiration by regulation of rate and tidal volume, or should the pulmonary ventilation be regulated by particular pressure changes determined in the airway?

It is, in our opinion, necessary that both factors be subject to regulation for controlled respiration, or at least that both the tidal volume and the phase pressures be known at any time during the administration of the anaesthetic. Whichever is used as the primary means of control, the other should have a reliable preset blow-off valve that releases when dangerous levels develop in the course of attaining the desired level of lung inflation.

If subatmospheric pressure is employed is the suction on the airway actually transmitted to the pulmonary alveoli? If so, does effective pulmonary ventilation continue even when tracheobronchial and alveolar secretions are present in abnormal amounts? Further, does a subatmospheric pressure phase in the respiratory cycle decrease the compliance of the lung, and require periodic hyperinflation (Radford et al., 1954)? In clinical practice, where there is a prolonged expiration time or

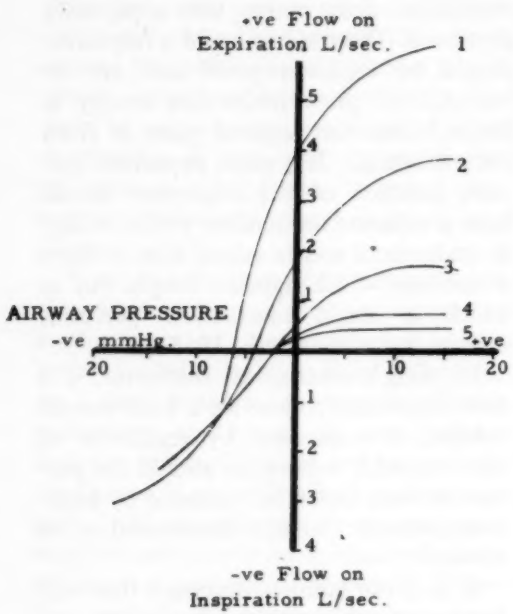

FIG. 12

Compliance–resistance curves in health and disease with chest wall intact and with pleura open.

$$\text{Compliance (C)} = \frac{\text{Volume of air entry (in litres)}}{\text{Pressure for air entry expressed in mm Hg}}$$

$$\text{Resistance (R)} = \frac{\text{Pressure for air entry}}{\text{Volume of air entry per second}}$$

(1) When chest wall is in resting position, lung holds 4 litres.

(2) Compliance of lung is an S-shaped curve, usually most steep in 2–4 litre range. Lung volume changes 120 ml per second for each mm Hg positive pressure when functional residual capacity (FRC) is normal, e.g. when normal individual is standing (R=1–3 mm Hg).

(3) Lung volume changes less for each mm Hg positive pressure when FRC is below normal, e.g. when normal individual is supine (R is increased).

(4) Patients with emphysema or obese patients whose lungs are at normal FRC, compliance is much reduced.

(5) If such patients as in (4) are placed in lateral or face-down position on operating table (FRC is reduced) at the end of expiration much less volume of air is in the lung and C-R curve is shifted to the left and flattened. Thus obtain much less change in alveolar ventilation with changes in airway pressure.

Note. (*a*) In normal lung, pressure change of 4 mm Hg provides tidal volume of 500 ml. (*b*) Airway pressure changes below atmospheric pressure ("negative") produce less change in airflow per mm Hg than above atmospheric pressure (" positive "). (*c*) As lung volume extends to inspiratory reserve volume all volume curves flatten, thus requiring ever increasing pressures for small volume changes. (*d*) In patients under anaesthesia with diaphragm paralysed by curarizing drugs the airway pressure is zero at end of expiration, but lung still holds 3–4 litres (1): 1.5 litres residual volume which cannot be exhaled, and 2.5 litres expiratory reserve volume which can be exhaled. When pleura is opened, major part of residual air can be expired or sucked out. (*e*) Cough, hiccough, laryngeal stridor, upper respiratory obstruction, bronchial secretions, bronchoconstriction, all increase resistance to airflow; while pulmonary vascular engorgement and pulmonary oedema stiffen the lung (decrease compliance) and resist lung inflation. These shift C-R curve to right and flatten the flow rise, as noted in curves (4) and (5).

other evidence of extensive trapping, the subatmospheric pressure should not be used after the pleura has been opened, unless there is visible evidence of adequate deflation of the lung during the expiration phase.

The anaesthetist should also have a number of physiological and pharmacological factors in mind when evaluating the management of these patients. Under the influence of hypnotic, analgesic and relaxant drugs, the measurement of pulmonary ventilation, as indicated by the rate, depth and minute volume of the patient's breathing or by that provided by the mechanical respirator, may be insufficient indication of the arterial pCO_2 unless a "steady state" exists (Elam et al., 1955). Therefore, is it essential to correlate the ventilation measurements with determinations of both arterial blood pH and pCO_2 and perhaps also pCO_2 of venous blood from the internal jugular vein (Lambertson et al., 1953)? All anaesthetic agents commonly employed, together with the increased concentration of oxygen provided during clinical anaesthesia, abolish to varying degrees the central and chemoreceptor mechanisms which support respiration. Respiratory stimulation and depression must therefore

be defined in terms of the economy of oxygen and carbon dioxide tension existing in the blood and alveolar air, as pointed out by Tenney (1956). For practical purposes, simple devices which indicate the arterial oxygen saturation and the carbon dioxide in the inspired and expired gas should be employed during all major anaesthetic procedures. An added consideration in long anaesthetics is the volume of nitrous oxide which has dissolved in the circulation and tissues. This quantity may be such that it would take many minutes to remove the major part of the nitrous oxide from the circulation. It is essential, therefore, that pulmonary ventilation be supported with a higher oxygen tension during the early post-operative period in order to avoid "diffusion anoxia" (Fink, 1955). Another way to avoid this condition is to gradually "wean" the patient off controlled respiration and discontinue the nitrous oxide during the last 10-20 minutes of an operation.

In reviewing current data available on ventilatory changes with mechanical respiration the following factors should be borne in mind in designing fixed pressure or fixed volume respirators. In the paralysed patient with healthy lungs the tidal air is proportional to the inspiratory pressure within the limits of 0.275 to 1.1 litres of tidal air and a peak pressure of 9 to 25 cm of water. Duration of inspiration influences tidal air optimally at about 1.5 seconds. At a peak pressure of 15 cm of water 0.48 litre of air enters the lungs in the first 0.7 seconds, and 0.19 litres enter in the next 0.7 seconds (Spalding, 1955). This is true only when the source of gas is supplied at an airflow of 40-60 litres per minute (Pask, 1955b). In order to circumvent this latter requirement in a practical respirator application of suction during the expiratory phase may be essential. The average curarized patient should therefore receive an adequate tidal volume with an inspiratory phase lasting between 1 and 1.5 seconds, and an adequate alveolar minute volume when the rate is 18 per minute. Lucas and Milne (1955) found that varying the relative lengths of the different phases of the respiratory cycle made no difference to carbon dioxide elimination, and if a pause were made between each breath the rate could not be increased sufficiently to maintain effective ventilation. This was not found in our clinical studies.

Nealon et al. (1955) showed that at a respiration rate of 20 per minute and a positive-negative mechanical respiration of +10 to +15 cm of water pressure, minute volumes of 15 litres per minute were easy to attain. It is the unusual patient who cannot be maintained at normal or slight alkalotic blood pH and pCO_2 levels with this ventilation, if the carbon dioxide absorber is operating efficiently. In our studies, where practically no pressure was lost between the respirator reservoir bag and the endotracheal tube through the use of semidistensible and nondistensible (tygon) tubes, it was evident that the lungs of almost all patients were adequately inflated and deflated by the pressures employed in positive-negative pressure respiration. This clinical observation was verified by the arterial blood pH, pCO_2 and oxygen content, and is logical to assume from airway pressure-gas flow curves of lung compliance (Fry et al., 1954; Brown et al.,

1954). In Nealon's study it was noted that ventilation was adequate and operating conditions were good with pressures of +15 mm Hg and −5 mm Hg, phases 1:2 and mean endotracheal pressures of 5 mm Hg, which produced a minute ventilation of 10 litres per minute. When the mean orotracheal pressure was 3 mm Hg, the surgeon observed that the lung was partially collapsed, and when the orotracheal pressure was 7 mm Hg, the surgeon considered that the lung was too tense or over-distended. When the phases were set at a 2:1 ratio, ventilation was much better though the lung was too tense with +15 mm Hg/–5 mm Hg. The lungs were satisfactory with pressures of +10 mm Hg/−5 mm Hg, giving 14 litres per minute and with pressures of +10 mm Hg/–10 mm Hg, giving 15 litres per minute. They noted that the greatest ventilation occurred when the ratio was 1:1 using +15 mm Hg/–5 mm Hg. Apparently acid-base homeostasis was well maintained with these three patterns using inflation and deflation of the lungs. They also found that the pCO_2 was raised in 85 per cent of cases during induction (17 out of 20 patients). The pCO_2 was markedly elevated at the time of intubation in 6 of 20 patients and fell to near-normal levels with the respirator in 18 of the 20 cases. This latter observation was also made with manually controlled respiration without the chest open (Buckley *et al.*, 1953).

Bjork and Engstrom (1955) and Elam (1955c) favour a fixed volume delivery. Elam contends that during anaesthesia and surgery the compliance of the lung changes, and therefore a fixed pressure is not suitable for delivering an adequate tidal volume. However, the compliance may either increase or decrease, perhaps indicating that the lung "needs" more or less alveolar ventilation. With the anaesthetic technique used in our study, the compliance probably increased markedly. This might indicate a much greater "need" for alveolar ventilation. However, the changes in either direction do not necessarily imply that a set volume should be delivered at all times under varying anaesthetic and surgical conditions.

The use of a fixed volume respirator may be a logical approach where bronchus blockers and endobronchial tubes are used to conduct gas to and from the normal parts of the lung. Otherwise provision for reinflation at increased pressures must be available to ventilate areas of lung with partial atelectasis which are discovered on opening the pleura, or which have been permitted to develop in an attempt to facilitate the surgical dissection. In this study, it was always possible to provide the volume of ventilation as predetermined and as found desirable during the pulmonary operation, without exceeding safe inflation pressures. Moreover, the Radford nomogram figure was greatly exceeded in all the cases in these studies. Theoretically, this assured a normal pH and pCO_2 as well as satisfactory oxygenation, even if varying degrees of pulmonary congestion with or without intra-alveolar or interstitial oedema decreased lung compliance. Even then, undesirable changes in pH sometimes occurred. These could usually be explained.

Normal oxygen figures found by Lucas and Milne (1955) when minute volumes as low as 1.5 litres, as sometimes encountered in patients in the supine posture for abdominal surgery, were doubtless due to

the " spike " flow of gases (Comroe, 1953). Kergin et al. (1948) found quite the reverse when the chest was opened. In patients with advanced pulmonary disease oxygen content of the blood is usually decreased, and when anaesthesia and thoracic surgery are superimposed the provision of increased oxygen tension in the inspired air appears to be essential if a near-normal tension in the blood is to be maintained. Some of the reasons for these disturbances are revealed by Rappaport's (1954) postulation of disturbed visceral function of the lung caused by pulmonary disease; Johnson's (1951) and Eckenhoff's (1955) findings on the effect of premedication with narcotics; the effect of the artificial pneumothorax and posture as found by Beecher (1950) and Etsten (1953); and the effects of circulating anaesthetic drugs as described by Watrous (1950), Taylor (1950), Gabbard (1952) and Buckley (1953).

It appears evident that to assure adequate alveolar ventilation, normal acid-base balance, and normal cardiovascular function, the surgeon must accommodate himself to a pressure-volume curve for lung inflation which extended experience proves best for the patient; and the anaesthetist must learn to adjust the respirator to the various needs of his patients and to varying operating conditions. The anaesthetist must also impress the surgeon working in the open thorax with two facts: *First*, in reducing the movement in the operative field to facilitate his operation, the surgeon must recognize that low oxygen levels and rising CO_2 tensions may be produced. The suboxygenation can usually be corrected rapidly, but high CO_2 levels may be most difficult to clear. Reduction of pressures which allow segmental and lobar collapse permit surface tension increases which may become almost insurmountable with short periods of high inflation—as evidenced by the necessity for prolonged efforts to re-expand the lungs. These efforts undoubtedly can cause extensive damage to the normal portions of the lung. *Second*, the surgeon should also recognize that opening a major bronchus and permitting massive leak from the airway must be of minimum duration, since here oxygenation must be maintained by insufflation. This permits considerable levels of carbon dioxide retention to develop (Whitehead, et al., 1949).

Physical principles which play an important role in the provision of optimum pulmonary ventilation are now well known to the anaesthetist. These include the necessity of providing an airway system which will maintain the lowest possible resistance to breathing that is mechanically possible (Orkin et al., 1954, 1956) and which circumvents the normal resistance encountered in the oropharynx (tongue, epiglottis, larynx and salivary secretions). To provide this requires the design of an anaesthetic gas machine with valves of very low resistance, gas flows which satisfy a full range of requirements for the instantaneous rate of inspiration and the avoidance of corrugations and sharp curves in the inflow limb of the ventilation circuit. For intrathoracic operations it is helpful to use nondistensible tubing from respirator to the anaesthesia machine and semidistensible tubing from the anaesthesia machine to the patient in order to avoid loss of volume or pressure in the mechanical circuit. The anaesthetic

machine should be joined to the largest size endotracheal tube which can be inserted without trauma. These factors remove the loss of a substantial volume of ventilation due to alternate ballooning and collapsing of the oropharynx. Thus, adequate ventilation may be provided at lower respirator pressures and volumes.

In considering the factors within the lung which affect pulmonary ventilation it is most essential to avoid reduction of the functional residual capacity (FRC) (Whitfield et al., 1950). According to Dubois et al. (1952) the FRC depends on changes in the blood buffers; oxygen and carbon dioxide content of the blood; and on the surface tension in the lungs. Reduced FRC results in more rapid changes in gas concentration in the lung. The changes with inhalation anaesthesia are more rapid, emergence from inhalation anaesthesia is more rapid, induced apnoea produces hypoxaemia more rapidly; while the arterial pH and pCO_2 have wider variations during the breathing cycle. Whitfield et al. (1950) and Fowler et al. (1950) have shown the changes in FRC with alterations of posture (see fig. 11).

The added effects of anaesthesia on FRC are still unknown. However, the anaesthetist must attempt to provide conditions which will allow a maximum volume of gas exchange in the lungs for each unit change in pressure. That is, the compliance of the lungs must not be permitted to fall because of pulmonary vascular engorgement and lung oedema, tracheobronchial secretions, bronchial and bronchiolar constriction, and inadequate muscular relaxation during controlled breathing. Increased compliance may be assured by using adequate amounts of drying agents (atropine or scopolamine), suctioning of the tracheobronchial tree at frequent intervals, by administering bronchodilators, and by maintaining adequate muscular relaxation. The surface tension changes due to small amounts of sticky secretions deep in the tracheobronchial tree can rapidly cause an adequate tidal volume to be distributed to an inadequate fraction of the total number of functioning alveoli. This must be avoided. It is also important to defer pulmonary surgery shortly after pneumoperitoneum, or else withdraw the air from under the diaphragm in order to reduce its ballooning into the operative field and thus compressing the lungs.

As the anaesthetist assists or controls the respiration of these patients and checks the circulatory status every few minutes, he may wonder about the disruption of physicochemical function that has occurred with induction of anaesthesia and production of surgical pneumothorax. Does the function of the lung under normal conditions really involve the intermittent and regular switching on and off of a suction device for inspiration, concurrent with the compression of a bellows (chest wall) and the elastic recoil of a balloon (lung parenchyma) for expiration, while the processes of pulmonary ventilation, gas distribution, gaseous diffusion, and capillary flow are represented as a "physico-mathematical image" (Arnott, 1955)?

Otis et al. (1956) have even considered the lung as a number of parallel pathways, each consisting of a compliance (C) and a resistance (R) in series, and by analogy to an electrical circuit they concluded that the distribution of ventilation would be

uninfluenced by changes in breathing frequency *only if* the time constants ($R \times C$) of the separate pathways were the same. If the time constants differed, the distribution of ventilation would alter with changes in breathing frequency. This would be accompanied by changes in overall mechanical behaviour of the lungs. Then compliance of the lungs would decrease and resistance in the airway would increase as the breathing frequency increased. Pulmonary compliance drops most and airway resistances increase most with increased breathing frequencies in subjects with bronchospasm or in patients with asthma and emphysema. It therefore appears important during anaesthesia to provide alveolar ventilation by the slowest rate of respiration which will provide adequate tidal exchanges without over-inflating the lung.

Rappaport (1954) is among the few who currently believe that a primary visceral function of the lung exists rather than a physical function only. The manifestations of this are most obvious when parenchymal lung disease is present or a major physiological change has been produced either, by diseases of the heart or by such acute conditions as pulmonary surgery or pulmonary infection. He makes two major assumptions: (1) there exists a special functional activity of the breathing surface structures which serve to adapt the diffusing surface of the lung constantly to the momentary gas exchange requirements of the body; and (2) this activity is of a type involving changes in quality (permeability) as well as in quantity (distribution) of the diffusing surface.

The mechanistic or physical concepts of pulmonary function are only now beginning to explain a purposeful correlation between pulmonary ventilation and circulation through all parts of the lungs and a correlation of diffusing capacity with momentary requirements of the body in health and disease (Comroe, 1953, 1955). For patients with pulmonary pathology or those undergoing any intrathoracic operation the anaesthetist should recognize that much higher rates of alveolar ventilation and much higher tensions of oxygen must be supplied if near-normal oxygenation is to be attained. This is necessary to compensate for the unknown extent of shunting of blood past normal lung, the shuntlike effect due to distribution difficulty in the emphysematous patient, and the shift of the oxygen saturation-tension curve to the right which causes diffusion difficulty when the patient is hyperventilated (Cournand, 1950; Perkins, et al., 1956). The solution of the problem of providing adequate alveolar ventilation when relaxant, hypnotic and analgesic drugs, respiratory paralysis and surgical pneumothorax are added to a disease state must require higher oxygen tensions and increased minute volume of ventilation in order to counterbalance the pathology present and abnormal physiology superimposed by the therapeutic procedure.

SUMMARY

Data which have been gathered during recent years clearly indicate that the management of all general anaesthetics requires assistance to the patient's pulmonary ventilation for all operative procedures. Adequate pulmonary ventilation should imply maintenance of oxygen

saturation of the arterial blood, elimination of the alveolar carbon dioxide to levels which maintain the arterial blood pH within normal range (7.35–7.45), and arterial carbon dioxide tensions between 35 and 45 mm Hg. This ventilation should also sustain or promote normal cardiovascular function as indicated by a stable blood pressure and pulse rate.

It is necessary to control the respiration when the pleura is opened, for otherwise the definition of adequate pulmonary ventilation cannot be fulfilled. The advantages and disadvantages of manual control of respiration have been noted. When diligently carried out with close attention to the patient to balanced anaesthesia, and to the operative procedure, most patients remain in a near-normal physiological state. The use of mechanical respirators is of considerable assistance if the inherent limitations imposed by lowered lung compliance and elevated airway resistance due to cardiopulmonary disease and the mechanical failings of present-day respirators are recognized. Current data contend that both volumes and pressures applied to the patient's airway must be considered for each individual patient if optimum anaesthetic care and management is to be provided.

CONCLUSIONS

As one views a procession of patients with normal and abnormal lungs, together with their lung function studies, and then subjects them to analgesic drugs and paralysis of respiratory muscles, both before and after surgical pneumothorax, one frequently becomes aware that pulmonary ventilation and respiration involve more than a static and dynamic mechanical phase (or an electric circuit); a physicochemical phase in the lungs and in the pulmonary blood flow; and a simple transport system via the systemic circulation. These may be the simple facts. However, the management of these patients to date has not proved a simple matter which can be reproduced easily by mechanical means. The major success has involved the substitution of another biological factor, namely, the alert hand of the anaesthetist. Until better mechanical devices are developed, the anaesthetist should continue to use manual control until the "hand" is no longer our most "educated" device.

In our position of fading darkness it is urgent for the clinical anaesthetist to stand close to the patient and to the rebreathing bag and view surgical pneumothorax with renewed interest and clinical acumen, for at present the mechanical respirator relegates his thoughts to pure physics, mechanics and mathematics. This furthers the trend described by Einstein and quoted by Rappaport: "Physics has often reduced the biologist into interpreting biological phenomena too primitively." Until more knowledge is procured, developed and simplified, the anaesthetist should stoop over the head of the operating table and still consider the lung and the physiological changes in cardiorespiratory function and acid-base homeostasis associated with its pathology as "the little black box" of Meneely's editorial "For Breath Too is Nutriment" (1955)

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CONTRIBUTION TO THE THERAPY OF MYOCARDIAL DEPRESSION CAUSED BY THIOPENTONE SODIUM

(Studied by high frequency cardiomyography)

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A FALL in blood pressure occasionally occurs during intravenous anaesthesia with various barbiturate preparations (Adams, 1944; Buhr, 1951; Duesberg and Schroeder, 1944; Wezler and Thauer, 1942; and others). Some authors have attributed this fall in pressure to a direct action of barbiturates on the myocardium (Johnston, 1936, 1938; Roth, 1935; Gruber, 1937, 1952). Others maintain that decreases in blood pressure in these circumstances are due to vasomotor reactions occurring in the peripheral vascular bed (Harris, 1951; Haynal and Held, 1950; Jacobi and Roemer, 1911; Nikolajev, 1948; Svec, 1953). However, convulsant analeptics, such as picrotoxin, leptazol, etc., have no satisfactory effect in these cases (Adams, 1944; Locket and Angus, 1952; Schoenwald, 1940; Stephenson, 1953).

On the whole, relatively little attention has been devoted to this question of the hypotensive effects of intravenous barbiturate anaesthesia, despite the fact that blood pressure levels may often fall by 20 mm Hg in normotensive patients. Any larger fall in blood pressure may have dangerous consequences especially in patients with latent or manifest coronary disease. The risk is also increased in patients in whom this effect of thiopentone anaesthesia is superimposed upon an already lowered blood pressure as, for example, during shock (Adams, 1944).

In the studies to be reported, there have been analysed more closely the factors causing lowering of the blood pressure during intravenous anaesthesia with sodium thiopentone and we have attempted to influence this decrease in pressure therapeutically. The effect of this therapeutic intervention on the depth and duration of anaesthesia has also been investigated.

METHODS

Experiments were carried out in a total of 15 dogs (weight 18–25 kg); 12 dogs under initial light thiopentone anaesthesia (30 mg/kg body weight) and 3 under initial chloralose anaesthesia (100 mg/kg). Mean arterial blood pressures were recorded from the femoral artery, using a mercury manometer. Simultaneous measurements of aortic blood pressures were taken with a condenser manometer (Hansen, 1949). In addition myocardial contraction was registered by means of high frequency cardiomyography registering changes of high frequency current, as measured across two electrodes, originat-

ing in changes of the impedance of the heart muscle (Froněk and Píša, 1956). The e.c.g. was recorded with an epicardial wick electrode moistened with saline.

In a series of six experiments 25–50 mg sodium thiopentone were introduced directly into a side branch of the left descending coronary artery, according to the method of Tennant (1935). This method was modified so as to introduce a fine nylon catheter into the artery through which test material could be injected. The advantage of this method lies in the fact that the blood stream carries the test solution injected in the left descending coronary artery into an intact area (where high frequency myography and e.c.g. electrodes are placed), and does not damage the area supplied by the descending branch, itself (fig. 1).

In a further series of experiments we investigated the effect of administering 10 per cent $CaCl_2$ on the duration and depth of thiopentone anaesthesia. The studies were carried out on rabbits weighing 2.5–3.5 kg. All animals were injected with sodium thiopentone 45 mg/kg at the rate of 25 mg thiopentone per minute. The length and depth of anaesthesia were estimated as described by Magnus (1922, 1926) and Girndt (1932).* A control group of 10 rabbits received thiopentone only. Twenty-four animals were given in addition $CaCl_2$ in dosages of 90 mg/kg immediately after completion of the thiopentone injection.

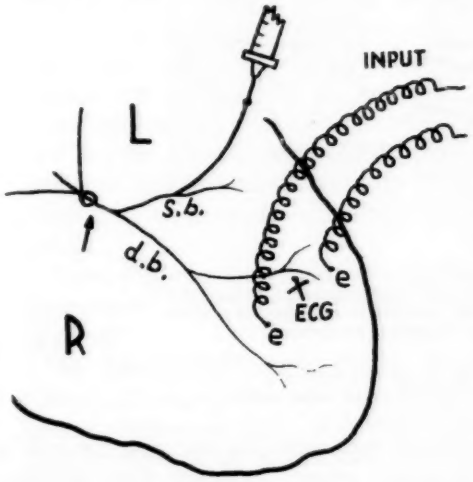

FIG. 1

Topical plan of the investigated area.
L=left ventricle, R=right ventricle, +=e.c.g. electrode, *e*=high frequency myography electrodes, *d.b.*=descending branch, *s.b.*=side branch of the coronary artery (left).

RESULTS

Effect of intravenous administration of thiopentone.

Thirteen dogs were given intravenous thiopentone in doses which caused lowering of the blood pressure to levels of about 30 mm Hg. Figure 2 shows the blood pressure course following intravenous injection of 500 mg of thiopentone. Comparable falls in pressure occurred in all 13 experiments. The simultaneous record of the aortic pressure and cardiac contraction is depicted in figure 3. In the particular record both the blood pressure fall and weakening of contraction after administration of thiopentone were very marked (fig. 3B).

One can conclude from these experiments that a weakening of myocardial contractility plays an important role in the hypotension under these experimental conditions.

* This method consists of observing a group of 19 different reflexes in consecutive 3-minute periods. This permits an estimation of the depth of narcosis. The termination of narcosis is defined by the time when all 19 reflexes are restored.

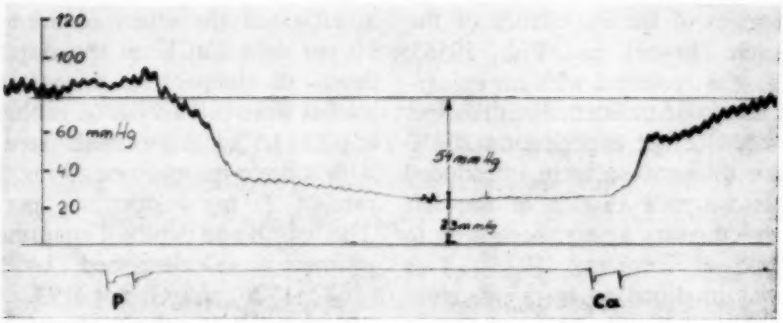

FIG. 2
Blood pressure (fem. artery) after thiopentone intoxication and injection of $CaCl_2$.

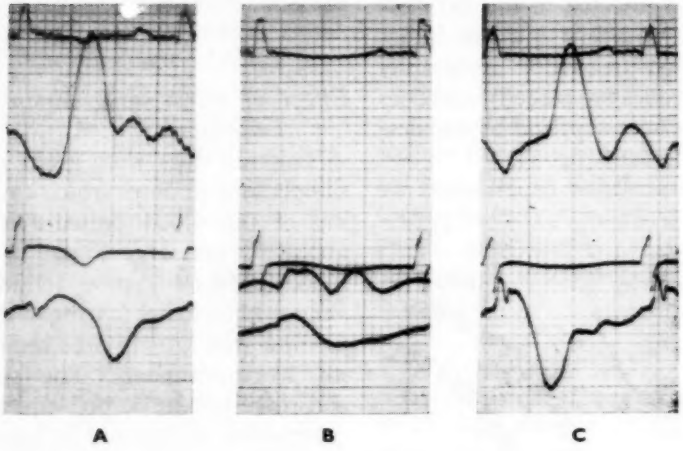

FIG. 3
Intravenous injection of thiopentone and $CaCl_2$.
Simultaneous record of blood pressure, and high-frequency myography (from above: standard lead II e.c.g., blood pressure from aorta, e.c.g. from the epicardium and high-frequency myogram).
(A) Control record.
(B) After intravenous administration of 500 mg of thiopentone.
(C) After intravenous administration of 5 ml of 10 per cent $CaCl_2$.

Effect of intracoronary administration of thiopentone.

The direct action of thiopentone on the myocardium was further investigated in another series of experiments, in which different concentrations of thiopentone (25–50 mg) were injected directly into a coronary artery. In figure 4 we see that after intracoronary administration of thiopentone the expected changes in contraction of the affected muscle do occur and the myographic curve is completely in-

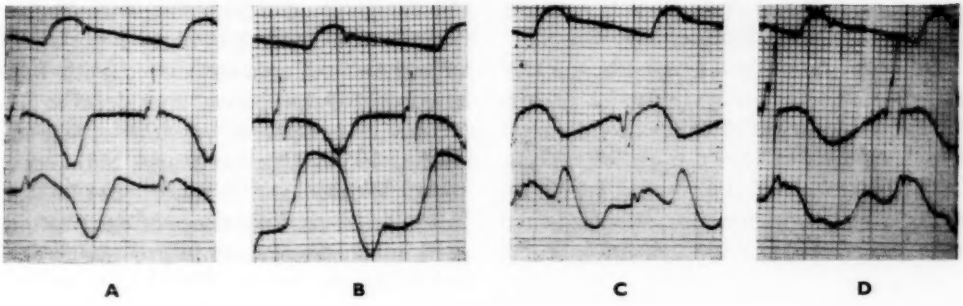

FIG. 4

Intracoronary injection of thiopentone and $CaCl_2$.
(from above: blood pressure from the aorta, e.c.g. from the epicardium and high-frequency myogram).

(A) Control record.
(B) After intracoronary injection of 50 mg of thiopentone.
(C) Seven seconds after the beginning of intracoronary injection of 2 ml of isotonic $CaCl_2$.
(D) Forty seconds later.

verted (fig. 4B). In other words, the damaged myocardial muscle undergoes aneurysmal dilatation during systole. It has to be added that the resulting myographic curve changes in this arrangement of the experiment (administration of the tested substance through the side branch) are due not only in consequence of the weakening of the affected musculature, but the alterations recorded from the damaged area are accentuated by the intraventricular pressure increasing during systole.

These findings show again that sodium thiopentone acts directly on the myocardium.

We have sought some means of reversing this depressant action of thiopentone on the myocardium. It is known that calcium stimulates myocardial contraction (Danielopolu, 1922; Beck and Mautz, 1937; Kunzová, 1941; Dale, 1952; Rothlin and Cerletti, 1952; Gross, 1953).

We therefore tried to abolish the effects of thiopentone on the myocardium with calcium. Figure 2 shows rapid restoration of the lowered blood-pressure following intravenous injection of 5 ml of 10 per cent $CaCl_2$. In 12 out of 13 trials, the blood pressure returned almost to original levels after intravenous administration of $CaCl_2$. In figure 3C are shown not only blood pressure changes following intravenous $CaCl_2$, but also striking alteration in myographic curves reflecting changes in the strength of myocardial contraction.

The results of intracoronary injection of isotonic $CaCl_2$, after thiopentone depression was already established, further convinced us that the hypotensive action of thiopentone is a direct one. Figure 4 illustrates a typical experiment in which the picture of myocardial dilatation was first evoked by intracoronary injection of thiopentone (fig. 4B). The rapid recovery of cardiac muscle function after $CaCl_2$ (administered via side branch) is evident from the myographic curves shown in figures 4C and 4D.

Effect of $CaCl_2$ administration on the duration and depth of anaesthesia.

In order to ascertain whether intravenous $CaCl_2$ had any influence on the duration and depth of thiopentone anaesthesia, we carried out tests on 34 rabbits. In the control group (10 rabbits), which received only thiopentone, anaesthesia lasted an average of 41.9 minutes (table I). A second group of 24 animals was given $CaCl_2$ immediately after thiopentone and in this group the average duration of anaesthesia was 35.5 minutes. The difference between the groups was not statistically significant ($p = 0.5$). The effect of $CaCl_2$ on the depth of thiopentone anaesthesia was also investigated. In table I are summarized the average lengths of time after thiopentone administration when the signs of various stages of anaesthesia appeared in the animals. Differences in the course of narcosis between the control group and the group receiving $CaCl_2$ were not significant.

TABLE I

	No. of experiments	Duration of the narcosis	Depth of the narcosis			
			IV	III	II	I
Control group	10	41.9 ± 9.3	8.8 ± 4.1	15.4 ± 4.8	25.0 ± 8.3	31.0 ± 7.9
After thiopentone $CaCl_2$ injected	24	35.9 ± 9.2	11.9 ± 4.1	18.4 ± 6.4	24.7 ± 7.7	29.6 ± 9.0
Statistical significance		t = 1.788*	t = 1.997*	t = 1.344*	t = 0.094*	t = 0.430*

* Not significant.

DISCUSSION

It is possible to conclude from the experiments, described above, that an important, if not the chief, cause of hypotension during intravenous thiopentone anaesthesia is a direct depressant action of this barbiturate on the myocardium. This conclusion is in agreement with recent experimental work, which has found anaesthetic collapse associated with falls in cardiac output with considerable increases in peripheral vascular resistance (Buhr, 1951; Duesberg and Schroeder, 1944; Wezler and Thauer, 1942). We fully realize that the doses of thiopentone used in our experiments are toxic. Our experiments were not planned to prove that decreases in blood pressure with dosages ordinarily given in clinical practice, come about in the same manner. Because of the unequivocal efficacy of calcium in restoring blood pressure levels in clinical trials (see below), we can postulate, however, that hypotension following usual doses of thiopentone are brought about by direct action on the myocardium. Furthermore, it would be very difficult to explain this therapeutic efficiency of calcium, which itself acts as a vasodilator (Rothlin and Cerletti, 1952) if hypotension during thiopentone anaesthesia were a result of vasodilatation occurring in face of an unchanged cardiac output. It is difficult to determine whether the therapeutic effects of calcium in our experiments can be ascribed to a tonic effect of calcium on the myocardium or to thiopentone detoxification by calcium in the body. If detoxification of thiopentone were in-

volved one would expect that calcium would influence narcosis also either by shortening the duration of thiopentone anaesthesia or affecting its depth. Summarizing the negative results of our experiments in this direction, we may hypothesize rather some interference by calcium with myocardial metabolism. It seems noteworthy to recall the findings of Govier et al. (1953) on the one hand and Mendel et al. (1939) and Nachmansohn (1940) on the other. They reported the cholinesterase-inhibiting action of thiopentone and the cholinesterase-activating action of calcium respectively.

SUMMARY

(1) A weakening of ventricular contraction during intravenous administration of thiopentone has been demonstrated with high frequency cardiomyography. A direct depressant action on myocardial muscle by this drug has also been demonstrated following its intracoronary administration.

(2) It has been found that falls in blood pressure caused by thiopentone are immediately reversible by the intravenous administration of 5–10 ml of 10 per cent $CaCl_2$.

(3) The intravenous administration of $CaCl_2$ affects neither the duration nor the depth of anaesthesia in rabbits.

(4) It has been emphasized that these findings may be of some importance by increasing the safety of intravenous barbiturate anaesthesia:

(*a*) in patients with latent or manifest ischaemic myocardial diseases;

(*b*) in patients in shock;

(*c*) in cases of accidental overdosage or when more toxic preparations are used.

ADDENDUM

We discussed our experimental findings with the staff of the Institute for Experimental Surgery, prague-Krč (Director Prof. B. Špaček). Up to the present, Dr. Keszler (1955) chief anaesthesiologist of the institute, has given $CaCl_2$ intravenously to 18 patients in whom the blood pressure fell on an average of 20–30 mm Hg during intravenous anaesthesia with Narcamon (isopraphyl-beta-bromyl-n-methyl-barbiturate sodium) or thiopentone sodium. In 16 cases out of 18, the blood pressure returned to original levels immediately after the injection of calcium. The operative procedure was then continued without further incident. Dr. Racenberg, from the same institute, working in a foreign country has also successfully tried the therapeutic method suggested by us in 50 cases.

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CORRESPONDENCE

BUTHALITONE SODIUM FOR INTRA-OCULAR SURGERY

Sir,—My experience of the use of "Transithal" brand of buthalitone sodium is, as yet, confined to two hundred administrations in many branches of surgery. The cases in which I have been most impressed with its advantages over other forms of anaesthesia are in the elderly patient undergoing an intra-ocular operation. In this group I have administered buthalitone sodium to forty patients undergoing operations for extraction of cataract, iridectomy, or iridencliesis; their ages ranged between sixty and eight-three years.

Premedication was with either papaveretum 1/6 grain (11 mg) and scopolamine 1/300 grain (0.22 mg) or morphia 1/6 grain (10 mg) and atropine 1/100 grain (0.65 mg). Induction was with "Transithal" brand of buthalitone sodium 600–800 mg in a 10 per cent solution, followed by gallamine triethiodide 40 mg and suxamethonium 30–50 mg. Anaesthesia was continued with nitrous oxide and oxygen via an oral intratracheal tube. Respirations were assisted as and when necessary. Further intermittent doses of suxamethonium were injected if and when required.

In none of these cases have any side effects from the use of buthalitone sodium been observed, except for momentary apnoea.

Postoperatively the most marked and constant feature has been the complete lack of euphoria or disorientation almost from the moment of regaining consciousness. Only three patients vomited, in each case less than 30 ml of fluid.

The addition of the small dose of gallamine triethiodide is helpful in reducing any coughing or retching on detubation and any immediate restlessness is without its full force. Thus reducing the danger of intra-ocular haemorrhage or leakage of vitreous fluid.

G. LAVERY EVANS
Bradford, Yorkshire

ATTRACTING THE UNDERGRADUATE

Sir,—I read Dr. Bryce Smith's paper in your June issue with pleasure; it contains much food for thought and action. I would like to suggest a further means of fostering undergraduate and postgraduate interest in anaesthesia. The many facets of the anaesthetist's work should constantly be made evident in everyday practice. Rather than a narrow routine in which frequently the chief variation is the patient's age or position on the table, he should be shown a variety of general anaesthetic agents and methods, spinal, epidural, field, brachial plexus blocks, etc., each used in the appropriate case. I feel sure that the student who does see a wide range of surgical anaesthetic techniques employed and also diagnostic and therapeutic blocks, active pre- and postoperative care and experimental and clinical research, will appreciate what an interesting specialty Anaesthesia is—or can be!

MARK SWERDLOW
Manchester

Brit. J. Anaesth. (1956), **28**, 373

CONTINUOUS SCIATIC NERVE BLOCK

BY

GILBERT GROSS*

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IN a previous communication, a new technique of continuous bilateral obturator nerve block was described. Drawing upon this experience, we decided to apply the continuous technique to a similar problem at hand.

Mr. W. N. is a 64-year-old white male who has had multiple sclerosis for approximately fifteen years. The usual classical findings of euphoria, nystagmus, intention tremor, spasticity of the lower extremities and urinary and faecal incontinence were present. For several weeks prior to our consultation, it was noted that the patient had developed severe spastic flexion contracture of the right leg below the knee associated with constant pain in this leg from the knee through the toes. Several decubitus ulcers had developed over the lateral and medial aspects of the right calf as a result of this contracture and were very difficult to treat adequately. Figure 1 shows the position of the right leg before sciatic nerve block. The dressing covers the ulcers.

When persistent force was applied, the leg could be extended to approximately 85 per cent of normal. When this point of 85 per cent below knee extension was reached, severe subluxation of the knee-joint was noted and further nontraumatic extension was not feasible. When the persistent extension force was released, the leg would immediately swing back to its original flexion-contracture position. In addition to the severe subjective pain suffered by the patient, this malposition of the leg increased the already prodigious nursing care programme.

The neurosurgical consultant felt that in view of the nature of the patient's illness, the severity of his pain, and the heavy burden upon the nursing personnel, a right sciatic nerve crush might be the simplest and most effective procedure to solve the problem.

In order to predict what effect sciatic nerve crush would produce, we elected to carry out a pharmacological sciatic nerve crush by means of a sciatic nerve block using a local analgesic agent. In addition,

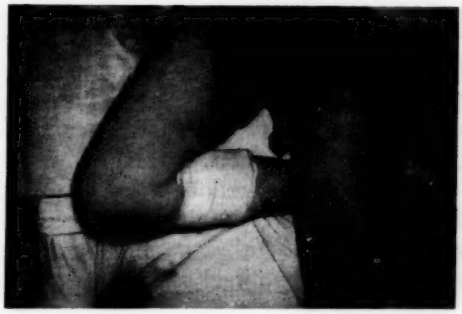

FIG. 1

Shows position of patient before sciatic block carried out. Dressing covers ulcers present over calf.

*Work done at Western Reserve Medical School.

sciatic nerve block appeared to be an excellent, simple, method of treatment of the patient's ulcers. In 1924, Taylor and Rice treated twelve patients with tropical ulcer of the lower third of the leg by open injection of the sciatic nerve. They used 5 to 10 ml of 15 per cent alcohol and obtained vasodilation in all cases so treated. The healing of the ulcer was hastened in every case.

ANATOMY

The sciatic nerve carries the bulk of the sympathetic nerve supply to the lower extremity (Gask and Ross, 1937; Engel 1944; Gask, 1933). The sciatic nerve is the terminal branch of the sacral plexus. It is a flat ribbonlike nerve about 12 to 14 mm wide and 4 to 5 mm thick at its origin. It is made up of ventral and dorsal roots of the fourth and fifth lumbar and the first, second, and third sacral nerves. The common level of union of these roots is at the anterior border of the great sciatic foramen below the pyriformis muscle. It descends between the greater trochanter of the femur and the ischial tuberosity through the posterior surface of the thigh to the level of its lower third.

After the sciatic nerve leaves the sciatic foramen it lies on the posterior surface of the ischium. It is accompanied by the small sciatic nerve and artery and is covered by the gluteus maximus muscle. The nerve is covered only by skin and fascia at the lower border of the gluteus maximus muscle and at the entrance of the nerve into the popliteal space.

NERVE BLOCK TECHNIQUE

The technique used is essentially that described by Moore (1953). The patient lies on the side opposite to the one being injected, with the knee brought up so that the thigh is flexed on the trunk at an angle of about 135 degrees. The midpoint of the uppermost portion of the greater trochanter of the femur is located and the posterior superior iliac spine is palpated. A line is drawn connecting these two landmarks. This line is bisected and a perpendicular is drawn to about 3 cm down from the midpoint. A skin weal is raised at this point and a $3\frac{1}{2}$ inch (9 cm) No. 22 gauge needle inserted in a downward direction until the needle point reaches the nerve when paraesthesiae are elicited. The paraesthesiae of the sciatic nerve are characterized by sharp, spraying, electric-like sensations which radiate down the leg to the toes, the heel, or the foot in general. The injection of the blocking agent is made when paraesthesia is obtained; 10 to 20 ml of the agent is most commonly used. The patient is forewarned that he will experience paraesthesia after which numbness of the leg will ensue.

CASE MANAGEMENT

Mr. W. N. was blocked daily by the above approach for seven days using 20 ml of 1 per cent lignocaine for each block. In each instance, after the block became effective, the leg became warmer, pain disappeared, superficial vessels became more prominent and the leg could be easily extended to its maximum 85 per cent of full extension, where it stayed for several hours. The decubitus ulcers began to dry up and show signs of healing. Although the leg would revert to its original flexion-contraction position after the block wore off, it soon became evident that it was becoming increasingly easier

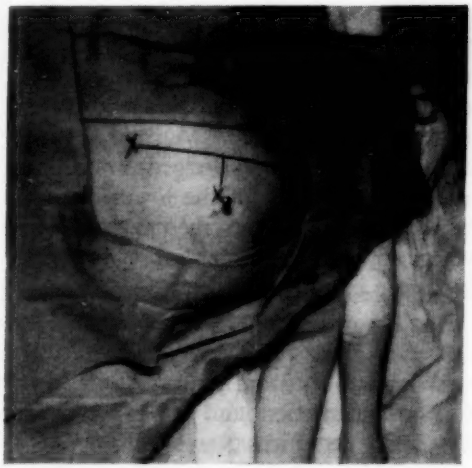

FIG. 2
Shows landmarks indicated by "x's" and number 16 Crawford needle in place ready for insertion of catheter.

to extend it again and it would remain so for a period of approximately one hour.

The eighth day we decided to try a continuous sciatic nerve block. Accordingly, a No. 16 Crawford extradural needle was inserted and sciatic nerve paraesthesiae elicited. Figure 2 shows the No. 16 Crawford needle in place before the catheter was inserted. "X" represents the midpoints of the posterior superior spine and greater trochanter of the femur. A ureteral type plastic spinal catheter was threaded through the Crawford needle to just beyond its tip. The Crawford needle was withdrawn carefully and the catheter left in place. Figure 3 shows the ureteral catheter in place prior to injection and adhesive strapping to patient; 20 ml of 1 per cent lignocaine was injected through this catheter slowly. It was necessary to inject slowly because of the moderate resistance offered by the tissues to this injection and it was feared that forceful, rapid, injection would serve only to dislodge the catheter from its proper placement. A good sciatic nerve block resulted. Figure 4 shows the almost complete extension and straightening of the right leg 15 minutes after the block was carried out. The catheter was strapped to the patient's thigh, care being taken to seal the area of exit of the catheter from the skin as tightly as possible to avoid possible contamination from urinary and faecal incontinence. The open end of the catheter was sealed with a 2 ml syringe which was also strapped to the patient. The patient was returned to the ward with 40 ml of 1 per cent lignocaine and the floor nurse instructed to inject 20 ml of the solution at bedtime and 20 ml the following morning. This was carried out with good results.

However, the following morning, shortly after the injection of lignocaine, the patient thoroughly soiled himself and the dressing over the sciatic nerve catheter with urine and faeces. It was felt that this

FIG. 3
Ureteral type plastic catheter has been inserted through Crawford needle and is ready for strapping to patient.

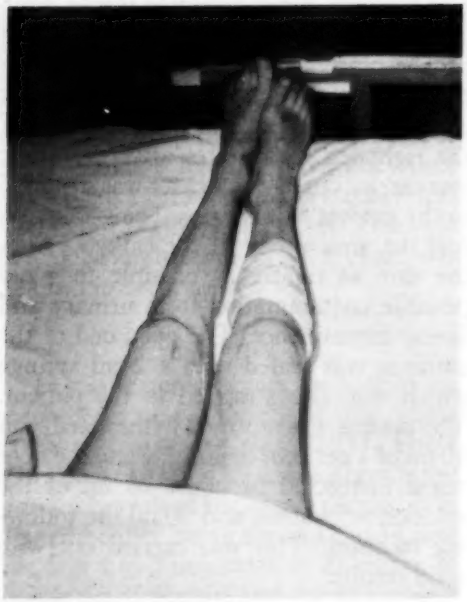

FIG. 4

This photograph shows maximum extension of blocked leg (bandage below knee). Leg almost completely straightened out.

occurrence would lead to infection and so the plastic catheter was removed and the patient again placed on daily sciatic nerve blocks. This case clearly pointed out that continuous sciatic nerve block is feasible in selected cases. This technique could be applied probably to patients with intermittent claudication (Marmer, 1952), patients with emboli lodged low in the arterial tree in one of the lower extremities, and to all other medical problems where prolonged unilateral sympathetic blockade is indicated.

SUMMARY AND CONCLUSIONS

A case of multiple sclerosis with flexion-contraction and unilateral lower extremity decubitus ulcers is presented. A method of successful continuous unilateral sciatic nerve block has been described and indications for further usage suggested.

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Brit. J. Anaesth. (1956), **28**, 377

A CLINICAL TRIAL OF BUTHALITONE SODIUM

BY

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INTRAVENOUS anaesthesia for the ambulant case has, in the past, left much to be desired, and has frequently been attended by such dangers as to preclude its use even by those skilled in intravenous techniques. In this paper, it is proposed to describe a clinical trial of a new ultra-shortacting thiobarbiturate in over 200 cases, most of whom have been ambulant. In particular, it is proposed to describe a technique which, in our experience, gives the most satisfactory result.

Buthalitone sodium, is the sodium salt of 5-allyl-5-iso-butyl thiobarbituric acid. It is a yellowish powder, easily soluble in water producing a solution having a pH of 10.5 in 10 per cent solution. It is an ultra-short-acting intravenous anaesthetic rapidly degraded, giving a short, trouble free recovery period with few side effects.

The age group of this series ranged from 2½ to 93 years, and included patients who had had such complications as cardio-vascular and respiratory lesions, pregnancy, epilepsy, mental deficiency and alcoholism.

Premedication was avoided in the ambulant cases; the only pre-operative measures taken were to ensure that the stomach and bladder were empty. In those inpatients in whom quick recovery of reflexes was considered essential, premedication was with either atropine 1/100 grain (0.65 mg) alone, or with atropine 1/100 grain (0.65 mg) and pethidine 50 mg.

TECHNIQUE

In the first 20 cases induction was with a 5 per cent solution; 2–4 ml were given rapidly followed by intermittent doses up to a maximum dose of 750 mg. This technique produced uncertain results, satisfactory anaesthesia being produced only at the expense of the recovery period, and is now used only for the poor risk and extremes of age.

Using a 10 per cent solution in a similar way, the results were more predictable, but still failed to produce a satisfactory uniformity.

In the remainder, the closed vein technique was used as described by Dr. John Halton (personal communication), that is a tourniquet is applied to the arm, a needle is inserted into a suitable vein, and a dose equivalent to 50 mg per stone (6.4 kg) of body weight up to a maximum of 500 mg is injected and the tourniquet released. The results produced by this technique give a more uniform plane of anaesthesia lasting 3–4 minutes with full recovery in 6–8 minutes, following which the patients are able to walk to the recovery room with a little assistance. Outpatients are allowed to leave after 30 minutes, being instructed not to drive a vehicle for 24 hours.

The main advantage of the closed vein technique is that a relatively high concentration of the drug reaching the brain in unit time produces a deeper plane of anaesthesia. The failure of the other techniques is considered to be due to lower concentration being too rapidly degraded before their full effect is produced. Further advantages are that a smaller dose is required to produce an equal plane of anaesthesia, but the recovery time is shortened.

The possible disadvantages of this "crash" technique are respiratory depression and a fall in blood pressure. These however, have been found to be of no serious disadvantage in the present series.

EFFECTS

(1) Induction time, broadly speaking, followed the pattern of other intravenous barbiturates, that is, it varied with the concentration of the drug, rapidity of injection, and the age, weight and physical condition of the patient.

(2) There was a fall in blood pressure in almost every case. Using the 5 per cent solution this fall in systolic blood pressure did not exceed 10 mm Hg; using a 10 per cent solution by "open-vein" technique in normotensive patients the fall was of the same order as with the 5 per cent solution, but in poor risks and in extremes of age it has been greater—the maximum fall recorded has been from 140/70 to 80/60 mm Hg. For this reason we reserve the use of 5 per cent solutions for these cases. Using the "closed-vein" technique, the fall in systolic blood pressure in normotensive patients was of the order of 10–25 mm Hg; the fall in diastolic pressure rarely exceeded 10 mm Hg. In all cases the blood pressure returned to normal within 3–5 minutes.

(3) The pulse rate varied from a mild tachycardia to a bradycardia, tachycardia being more noticeable with the more rapid administration of the drug, but in no case did the pulse rate exceed 100 beats per minute.

(4) There was no respiratory depression using a 5 per cent solution. Respiratory depression was most marked with the "closed-vein" technique and amounted, on occasion, to a momentary apnoea, but in no case did it give rise to any anxiety nor had oxygen to be administered to combat it. The absence of marked respiratory depression made the continuance of anaesthesia with inhalation techniques extremely easy. Cyanosis was not seen in any case.

(5) Recovery time seemed to be in inverse proportion to the rate of administration in the dosage recommended. However, this does not apply to the very young, whose recovery time was considerably longer. In doses exceeding 500 mg the recovery time was significantly prolonged and, therefore, the main advantage of this drug tended to be lost.

(6) There was no apparent excess of salivary secretions.

COMPLICATIONS

The commonest complication we have encountered has been hiccough. This occured in 10 per cent of cases, and being transient required no active treatment.

Nausea occurred in 5 per cent of cases, and vomiting in 1 per cent, all these cases having had premedication.

Bronchospasm or laryngospasm have not been seen.

There have been two cases of perivenous injection, both in the antecubital fossa. One patient received 1 ml of 10 per cent solution extravenously and presented symptoms of marked tissue irritation which was followed by limitation of movement, and a patch of anaesthesia developed around the site of injection, in spite of the immediate injection of 5 ml of 1 per cent procaine with hyalase. This patient recovered completely in seven days.

In the other case, the extravenous injection was of a few minims of 10 per cent solution, and the patient complained only of pain at the site of injection, which disappeared after a few minutes.

We can conclude from the above that buthalitone sodium might produce intense arteriospasm with its sequelae if given intra-arterially.

Delayed recovery has been seen in 5 per cent of the cases; most of these have occurred when the slower techniques were used or the maximum dose of 500 mg was exceeded.

INDICATIONS

The principal indication for the use of this drug is to take advantage of its short recovery period. This being so, we have used it, with outstanding success, in the following cases.

(1) *Dental Department.*

For chair patients buthalitone sodium by itself or buthalitone–nitrous oxide–oxygen sequence provides a pleasant trouble free induction, adequate anaesthesia and a rapid, smooth recovery, thus fulfilling the requirements of both the dentist and anaesthetist.

In particular, the chronic alcoholic or very nervous patient, those with a cleft palate or who are persistent mouth breathers and who might be difficult to induce with nitrous oxide and oxygen alone, have presented no difficulty when buthalitone induction has been used.

For more extensive oral work in the operating theatre the drug is eminently suitable, as it ensures a rapid return of laryngeal and pharyngeal reflexes.

(2) *Orthopaedic Outpatients.*

For orthopaedic manipulations buthalitone by itself used with the closed vein technique often provides sufficient relaxation. Occasionally, however, a small dose (25–30 mg) of suxamethonium is necessary.

(3) *Casualty Department.*

A smooth trouble-free induction afforded by this drug is an obvious advantage in the treatment of such conditions as the incision of paronychiae, whitlows, small abscesses, etc., which are normally dealt with as outpatients.

The use of this drug has been deliberately avoided in the treatment of abscesses around the mouth and throat because, although apparently less vagotonic than thiopentone, we are not yet satisfied that this drug is completely safe for such operations.

(4) *Obstetric Department.*

Here the drug has been used in breech presentations to facilitate the delivery of the aftercoming head. The mother has, on each occasion, been fully co-operative for delivery of the placenta.

It is felt that buthalitone may have a place in anaesthesia for Caesarean section, in those cases where there are signs of foetal distress, but our experience is,

as yet, insufficient to be more definite on this point.

The drug has also been used in anaesthesia for minor gynaecological procedures.

Buthalitone may have a place in other fields, such as bronchoscopy, electro-convulsive therapy.

CONCLUSIONS

It is felt that the uses of this drug and its possible place as an anaesthetic agent can best be illustrated by comparing it with the more commonly used thiobarbiturates. Compared with thiopentone and thialbarbitone, it has the following advantages:

(1) There appears to be less respiratory depression, and, therefore, it is easier to proceed to other inhalation techniques.
(2) There appears to be less cardio-vascular upset.
(3) It appears to be less vagotonic.
(4) It is more rapidly degraded.

It is, therefore, overall less toxic, and must be considered a safer drug.

Its main indication is for the ambulant case. In this category there appear to be very few definite contra-indications to the use of this drug. Cases where thiopentone would be administered with trepidation, even by the expert, have been anaesthetized with no untoward effects, as, for example, in patients with chronic bronchitis, asthma, hypertension, and rheumatic carditis, although the importance of these complications has not been minimized. It is not recommended that the normal standard of caution and care used in the administration of any anaesthetic should be reduced in the least, nor does the skill of the administrator require to be any less.

The rapid recovery period compared with other thiobarbiturates avoids congestion of outpatient departments and dental surgeries, patients being able to return home after thirty minutes. It should be pointed out here that part of this advantage may be lost by pre-operative sedation.

The main disadvantage of buthalitone is that it is a poor basal narcotic. For this reason it is felt that, for major surgery, this disadvantage outweighs its possible advantages, except in the poor risk and in those cases where the rapid return of the laryngeal reflexes is of paramount importance.

SUMMARY

The clinical trial of a new ultra-short-acting thiobarbiturate in 200 cases is described.

An additional technique to those already in use is detailed.

Its use mainly for ambulant cases in various departments is suggested.

Its advantages and disadvantages over other barbiturates are discussed.

ACKNOWLEDGMENTS

We would like to thank the Surgeons of the various Departments at Broadgreen Hospital and Mill Road Infirmary, Liverpool, for permission to use this drug on their patients.

We would also like to thank Messrs. May & Baker Limited for the supplies of buthalitone sodium (Transithal Brand).

Brit. J. Anaesth. (1956), **28**, 381

DENTAL PROTECTION DURING ELECTROCONVULSIVE THERAPY

BY

DAVID L. SCOTT

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MOST articles on e.c.t. make no mention of what shall be used to protect the teeth during the mandibular contraction. Some authors, however, mention the use of such things as spatulae, rubber hose piping, gags, and ring pessaries.

While such equipment may be adequate in the "normal" mouth with plenty of even, strong, and firm teeth, it is quite inadequate for the proper protection of valuable dental work.

When designing a dental protector, the following points ought to be taken into consideration:

1. Soft consistency.
2. One standard size.
3. Mask can be placed on face with protector still *in situ*.
4. Easy to insert and remove.
5. No risk of nipping lips or tongue between protector and teeth.
6. No tendency to jump out during shock.
7. Incapable of falling into pharynx of an unconscious patient.

* E.C.T. carried out at Sidsjöns Sjukus, Sundsvall.

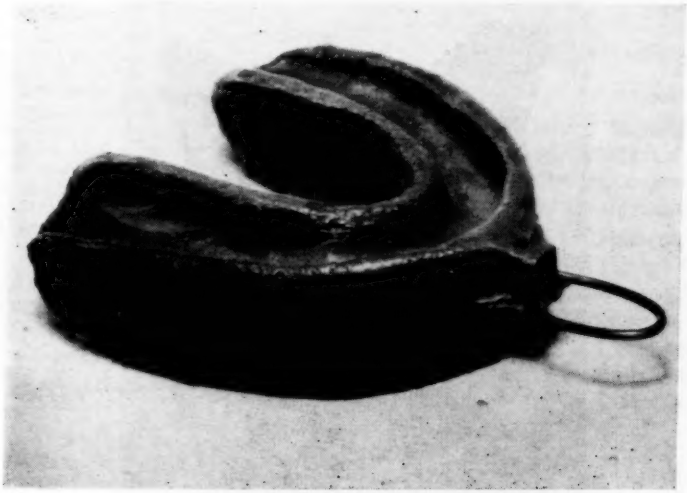

FIG. 1
New "protector".

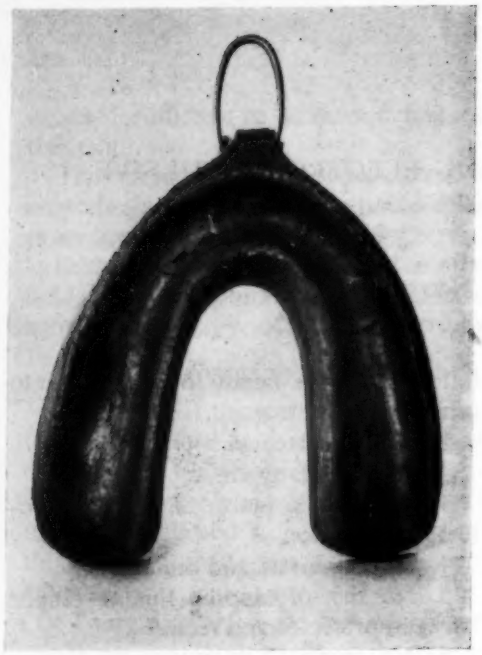

FIG. 2
New " protector ".

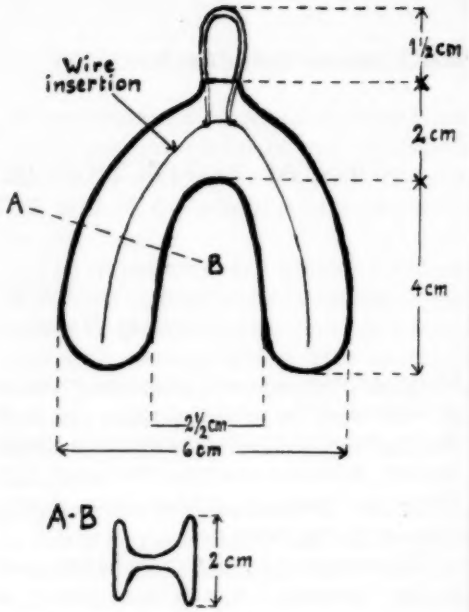

FIG. 3
Dimensions of new " protector ".

FIG. 4
Hård's " Elprotect ".

8. Distribution of pressure during shock over as many teeth as possible (i.e. less pressure per tooth).

9. Offer real protection to patients with extensive frontal bridges and crown caps.

10. Suitable if only a few scattered teeth.

11. Easily sterilized.

It will thus be seen that the usually mentioned items fall far short of the ideal.

Suggested new protector.

For some time I have been using a new type of protector, illustrated in figures 1 and 2. It is constructed of soft dental rubber and has a wire moulded in it which also forms the handle—essential for easy removal from the mouth. It is pliable, so can fit any adult mouth. The dimensions are given in figure 3, which also illustrates the H-shaped section.

Comments.

The only person I can trace who has previously designed a proper protector is Hård. He called it the "Elprotect". He must be given full credit for originally raising most of the points in design mentioned above. As his article is in Swedish, however, these points I have repeated and a photograph of his "Elprotect" is reproduced in figure 4, for the convenience of readers. I have used his protector many times and find it excellent. However, it jumps out during the shock if the mandible is edentulous, and does not seem as ideal as mine when extensive bridge work is present, as is common in Sweden—even in mental patients.

The "protector" was made for me by Messrs. Medical and Industrial Equipment Ltd., London.

REFERENCE

Hård, G. (1954). *Svenska Läkartidn.*, **51**, 1422 (English summary on p. 1425).

BOOK REVIEW

Acta de l'Institut d'Anesthésiologie. Tome 4, 1956. Published by Librarie Arnette, Paris.

This contains the lectures of the advanced course in Anaesthetics given by a number of authorities on their different subjects. There are thirteen of them, covering a wide variety of subjects. Are you a physiologist? Then you will be interested in what Professor Schapira has to say on the function of haemoglobin in respiration. Are you a pharmacologist? Then the articles by Professor Levy on the duration of action of the barbiturates and that on noradrenaline by Professor Baumann will be of some immediate concern to you. Dr. du Bouchet treats of cardiac syncope and Dr. Damoiseau of prolonged inadequate respiration, both of great interest to the practical anaesthetist, the man of action. The administrator will find food for thought in Professor Moulonguet's article on the housing of the surgical and anaesthetics service of a hospital. I have only mentioned six of the lectures, but all of them are of interest to the anaesthetist who wishes to be more than a technical expert, however skilled.

E. Falkner Hill

SOCIETY NEWS

LIVERPOOL SOCIETY OF ANAESTHETISTS

At the Annual General Meeting of the Society held at the Liverpool Medical Institution on Friday, May 11, 1956, the following Officers and Members of Committee were elected.

President	Dr. Hilda M. Garry
Vice-President	Dr. George R. Hopper
Hon. Treasurer	Dr. George McLoughlin
Hon. Secretary	Dr. John B. Hargreaves
Committee	Dr. J. R. Esplen
	Dr. Ruth Dovey
	Dr. J. Marchant

Brit. J. Anaesth. (1956), **28**, 384

MAGNETIC RACK ON ANAESTHETIC APPARATUS

BY

DAVID L. SCOTT

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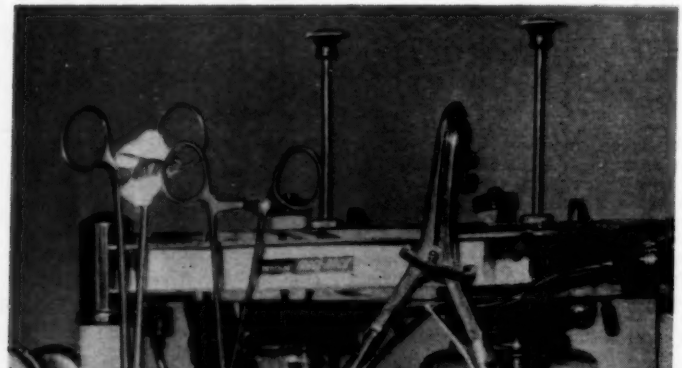
THE photograph shows how a Prestige "Magi-Rack" has been attached to a Boyle's apparatus. Gag, tongue forceps, etc., are thus instantly available and space is gained on the table. It is also particularly easy to check the presence of these items before beginning an anaesthetic—their position acting as a reminder to beginners. It will be noted that it is impossible to attach an ether vaporizer water jacket—a possible advantage, as this eliminates any possible risks of this attachment (Hewer, 1953).

A similar rack fixed to a Devanaest has proved even more useful in dental work where two gags are often in use and speed is essential.

When fitting, it is important to interpose a nonmagnetic material (e.g. fibre block) between the rack and the anaesthetic apparatus.

REFERENCE

Hewer, C. L. (1953). *Recent Advances in Anaesthesia and Analgesia*, 7th ed., p. 95, London: Churchill.



ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

JOHN SNOW, M.D.
Licentiate of the Royal College of Physicians

(*Continued from page* 236)

Case 34 occurred on October 20th, 1853, a few days after the last. The patient was a young woman named Ann Smith, aged 22 years, under the care of Mr. Paget in St. Bartholomew's Hospital, who was about to apply the actual cautery to a sore of cancroid nature in the vagina. She was a stout, florid young woman, formerly of dissolute habits, but apparently in perfect health, with the exception of the local ailment. She had been put under the full and prolonged influence of chloroform a fortnight previously for the application of the cautery, without the occurrence of any untoward symptoms whatever. The chloroform was administered by Dr. Black, one of the assistant physicians.

"The usual form of inhaler was employed,—a padded metal cup, fitting over the nose and mouth, and supplied with valves. A drachm, by measure, was first poured on the sponge, but as the administration did not immediately commence, a considerable part of this was no doubt wasted; after a short inhalation, a second drachm was supplied, and subsequently the further quantity of half a drachm. The patient had gone through the usual stages of excitement, etc., and the last dose was scarcely used, as she sank off, almost immediately after its application, into a state of complete insensibility, unattended by any alarming symptoms. About five minutes had been occupied by the inhalation, and probably not more than a drachm and a half of the fluid really inhaled. The apparatus was now removed from the face, and the patient having been drawn into the proper position, Mr. Paget was about to commence the operation, when Dr. Black, who throughout had kept his finger on the pulse, noticed it to have become extremely weak and fluttering. Almost immediately afterwards, the patient's countenance was observed to be dusky, turgid, and congested, and the respiratory movements began to be performed at long intervals, and by slight catching efforts. No time was lost; cold water was at once dashed on the thighs, face, and breast; and, the failure of the respiration becoming shortly complete, Mr. Paget immediately began artificial insufflation of the lungs, by alternately blowing into the nostrils, and compressing the chest. Just before commencing this process, Mr. Paget had ascertained, by drawing the tongue forwards and examining the glottis with the finger, that the epiglottis was not pressed down."

Other means were employed, but no

further signs of life appeared. It is further recorded that, "immediately after the first alarming symptoms, the pupils were of the medium size, neither contracted nor dilated. All efforts at respiration ceased about two minutes after the first indications of failure; the pulse, however, as a very feeble flutter, was felt occasionally for at least two minutes later."*

At the autopsy, performed by Mr. Paget, twenty-two hours after death, "the thorax was first examined, and nothing whatever abnormal could be detected in any of the viscera; the lungs were healthy and crepitant in every part; their posterior lobes were not more congested than is seen in almost every examination; the heart, collapsed, but not contracted, and containing a small quantity of fluid blood in each cavity, was of normal size and proportions, in every respect, and its muscular structure, examined by the microscope, showed no degeneration. . . . The brain, its sinuses, ventricles, etc., were all carefully examined and neither in texture nor quantity of blood was anything abnormal detected."†

Although the failure of the pulse was the first symptom of danger in this case, it continued to be felt as a very feeble flutter for about four minutes, so that the heart was not so completely paralysed as in most of the fatal cases. It must, however, have been so far paralysed as to be past recovery.

Case 35. Professor Dumreicher related a case of death from chloroform at the meeting of the Vienna Society of Physicians, held on November 16, 1853. The patient was a young man, aged nineteen in somewhat feeble health, who inhaled chloroform in the recumbent position, in order to have his anchylosed knee-joint forcibly extended. It was inhaled from a vessel resembling a snuff-box, which was held to the nostrils. "The inhalation was continued for fifty seconds, and the patient had spoken a few seconds previously, when Professor D. observed that the pulse had become frequent and undulating. He immediately suspended the administration of the anæsthetic. Trismus occurred; the respirations became irregular; the face turned livid, and he foamed at the mouth." The measures which were employed included the abstraction of eight ounces of blood from the jugular vein, but they were of no avail. He only once made a feeble attempt at inspiration.‡

Case 36 occurred in the practice of Dr. Wüstefeldt of Neustedt. "A young girl, thirteen years of age, had on the dorsal region a voluminous lipoma, which extended from the last dorsal vertebra to the crest of the ilium. . . . One drachm of chloroform was employed. As soon as insensibility was manifested, the operation was commenced, but scarcely had the surgeon divided the skin, when the girl, yielding to the laws of gravity, fell suddenly forwards on her chest. Dr. Wüstefeldt, struck by the phenomenon, which he had witnessed before under similar circumstances, immediately desisted from operating, and strove to restore the patient to life: but every effort was

* Medical Times and Gaz., 1853, vol. ii, p. 449.
† Ibid., p. 450.
‡ Edin. Monthly Jour., vol. xix, 1854, p. 372.

useless, and, in the course of a few minutes, it became evident that she was dead."*

Further particulars are not given; but as the patient died suddenly, when the surgeon had scarcely divided the skin, it must be admitted that he was, in all probability, correct in attributing the event to the chloroform. The patient usually yields to the laws of gravity when only partially under the influence of chloroform, and it seems surprising that the operation should have been undertaken without placing the patient in the horizontal posture. The proper position of the patient, when a large tumour of the back is to be removed, is to be lying almost flat on the abdomen, the head being a little turned on one side, so that it rests with one ear on the pillow.

Case 37. Jane Morgan, aged fifty-nine, died whilst inhaling chloroform in the Bristol Infirmary, on January 21st, 1854. She was moderately stout, pale, but not otherwise of unhealthy appearance. "The stethoscopic indications were favourable, the beat of the heart was natural, and the air passed freely throughout both lungs; but the chest movements on the right side were not quite so free as on the left." Chloroform was ordered by Mr. Harrison, the senior surgeon of the Infirmary, with the intention of attempting to reduce a dislocation of the humerus of eight weeks' standing. "Having taken no food since her breakfast, she commenced the inhalation of one drachm of chloroform, at 2 P.M., in bed in her ward, under the superintendence of Mr. Hore, the house-surgeon. Nothing unusual occurring in the patient's general condition during inhalation, a second drachm, in about five minutes from the first, was poured upon the sponge, and the inhalation was continued. Almost immediately after the addition of the second drachm, the chloroform was withdrawn, as the patient's breathing became stertorous; and immediately afterwards her pulse, which had hitherto continued pretty firm, was suddenly imperceptible, the respiration ceasing at the same time. The pupils were not dilated." Various measures were promptly resorted to with the hope of restoring the patient; but there were no further signs of life, unless "some convulsive efforts of the respiratory muscles," under the application of galvanism, be so regarded.

At the examination of the body on the following day, the right pleura was found to be adherent. The lungs were healthy in structure, but gorged with dark fluid blood. There was about an ounce of fluid in the pericardium. There was a small quantity of fluid blood in each of the cavities of the heart. For the length of an inch from their commencement, both coronary arteries were much dilated, and studded with atheromatous and bony deposits. The muscular structure of the heart was examined under the microscope by Dr. William Budd, and a considerable proportion of the fibres were found in a state of incipient fatty degeneration. It was learned, after her death, that she had been subject to occasional attacks of fainting.*

Case 38. A death from chloroform occurred in the Hôpital St. Antoine, at

* Med. Times and Gaz., 1854, vol. i, p. 19, from Med. Zeitung von den Vercine für Heilkunde in Preussen, No. 44, Berlin, Nov. 2, 1853.

* Association Med. Jour., 1854, p. 109.

Paris, in the spring of 1854. The subject of this was a woman aged forty, on whom M. Richard was operating for the removal of a uterine polypus. The surgeon placed the patient in the horizontal posture, and administered the chloroform on a compress of lint. She became insensible in two minutes, having first been excited so that it was necessary to hold her. M. Richard moved the patient to the edge of the bed, gave the compress containing the chloroform into the hands of an assistant, and commenced the operation, which was likely to be of short duration. He had almost completed it, when he was apprised by an assistant, who had been set to feel the pulse, that it had ceased to beat. He sought for it himself, but found that it did not beat. The face was extremely pale; a slow respiration still continued, but soon ceased; and the measures which were used with the hope of restoring the patient were of no avail.*

At the examination of the body all the organs were found in a healthy state. The right cavities of the heart and the great veins contained a considerable quantity of blood, and the left cavities of the heart a small quantity. The blood was everywhere fluid.†

Case 39. A patient, named Mrs. Harrup, died at Sheffield from the effects of chloroform administered with the intention of removing a cancerous tumour of the left breast. The age of the patient was forty-five, and she was stated to be in good health, excepting the local affection.

"The chloroform was administered with more than the usual precautions. After the inhalation had gone on without any effect for twenty minutes, it was thought that possibly different chloroform might succeed, and one ounce was accordingly procured from the public dispensary. After the inhalation had been conducted with the fresh chloroform about twenty minutes, the usual effects of the vapour began to manifest themselves. The pulse, which was 136 before any chloroform had been given, and had been very gradually decreasing in frequency while it improved in strength, was now about 104. At this moment muttering—half articulate delirium—came on, but ceased in a few moments, and was immediately followed by conclusive signs of the satisfactory action of the chloroform. Dr. Law now desired Mr. Wright to begin the operation; but before he could do so, Dr. Law, seeing an alarming change in the countenance of the deceased, cried, 'Stop, Mr. Lewis, how is the pulse?' I replied 'It is gone.'" After stating the means which were used with a view to resuscitate the patient, it is added that the heart had ceased to beat, and that, after a few short and laboured inspirations, life became extinct.

At the examination of the body, the cartilages of the ribs were found to be ossified. The heart and lungs were perfectly healthy, but the lungs were in a congested condition. There was an extravasation of blood in the spinal muscles, and a little blood in the spinal canal, in what part or between what structures is not stated.‡

Case 40 occurred in the Lock Hospital, London, in May 1854. Walter Hollis, a tailor, aged eighteen, had been under

*L'Union Médicale, 1854, p. 171.
† Ibid., p. 187.
‡ Association Medical Journal, 1854, p. 315.

treatment for sores within the prepuce, and these having healed, he was about to undergo the operation for congenital phymosis. He had been of dissolute habits, and exhibited a pale cachectic appearance.

"The inhaler used was a simple mouthpiece by which the nostrils are left uncovered. About two drachms of the fluid were poured into the instrument. After about six minutes inhalation, insensibility seemed to be coming on, and at this moment the pulse was ascertained to be of good volume. Nothing whatever had occurred to indicate the impending danger, when, after a few more inhalations, the pulse suddenly failed, became quite imperceptible, and the countenance assumed a pale and leaden hue. The inhalation was immediately stopped, and attempts to resuscitate, by means of striking the chest sharply with a wet towel, applying ammonia to the nostrils, and by artificial respiration, were at once commenced. These were employed for three or four minutes before any signs of life were perceived; but, subsequently, the pulse was again to be felt, and spontaneous respiration was renewed. Artificial respiration was desisted from on the occurrence of these signs of returning life, and for upwards of ten minutes the chest continued to fill regularly, and the pulse beat at a rate of from 40 to 50 in the minute; the countenance of the patient also much improved, and even assumed a slight flush. After the expiration of, perhaps a little more than ten minutes, however, these indications of returning vitality again disappeared, the pulse and respiratory efforts simultaneously ceased, and the countenance became deathlike. Artificial respiration and the other means were again adopted, but this time without the slightest success. . . . Post-mortem examination on the next day shewed great venous congestion within the cranium; the lungs were also somewhat congested. The heart was slightly enlarged, and the ventricular parietes were thinned; in the muscular fibres the microscope detected decided fatty degeneration. The blood was universally fluid."*

The partial recovery of the patient is a remarkable feature in this case, and it is difficult to explain why he did not recover completely. The number of the pulsations during this partial recovery is mentioned, but not their quality, and I cannot help supposing that the pulse must have been extremely weak, as well as slow, at this period. The ten minutes during which the pulse and breathing returned is mentioned with the qualifying term of "perhaps", which leads to the supposition that it was not noted by the watch or clock, and under such circumstances of anxiety and suspense, the time might be very much overrated. The slight fatty degeneration of the heart might probably interfere with the complete recovery of the patient, after this organ had once been paralysed by the chloroform.

Case 41 took place on July 13th, 1854, in the Middlesex Hospital. The patient was a stout, muscular, and florid man, 65 years of age, on whom Mr. De Morgan was about to perform amputation at the upper part of the thigh, on account of a large malignant tumour growing from the inner side of the femur.

"Chloroform was administered by Mr.

* Medical Times, 1854, vol. i, p. 572.

Sibley, the registrar to the hospital. Snow's inhaler was employed. The quantity at first placed in the inhaler was rather less than two drachms, and another drachm was added eight minutes afterwards. The patient inhaled the chloroform without difficulty, and went through the usual stages; at the end of about ten minutes violent spasm was induced; this continued about three minutes, and then somewhat abated. The pulse, which had risen to about 120, descended to 70, having a full, steady, and deliberate beat. The pupils, which had been much dilated, became less so. The respiration continued free and deep, but not stertorous. The colour of the face remained good.

"At this moment, which was between thirteen and fourteen minutes from the commencement of the inhalation of the chloroform, the pulse gave a few rapid and irregular beats, and then ceased. Respiration, which, as has been stated, had been going on freely, ceased simultaneously. The face became suddenly pallid and deathlike. The inhaler was removed instantaneously, and cold water dashed on the face. Mr. Sibley immediately commenced to carry on artificial respiration, by applying his mouth to that of the patient, and inflating the lungs. The period that elapsed between the sudden cessation of the pulse and the inflation of the lungs was only a few seconds. After a few inflations, there appeared to be a slight effort at inspiration, but this was the only sign of life discovered after the syncopal attack. Galvanism was in operation within two minutes after the cessation of the pulse.

"An examination of the body was made by Dr. Corfe forty-eight hours after death. In the head nothing particular was discovered; the brain was firm, and rather more vascular than natural; the blood in the sinus was partly coagulated; the heart was rather larger than natural, and was extremely loaded with fat, especially on the right side, where fat formed three-fourths of the thickness of the wall of the ventricle; the muscular tissue was extremely pale and soft, and exhibited both to the naked eye, and the eye assisted by the microscope, an extreme degree of fatty degeneration; the blood in the cavities of the heart was firmly coagulated; on both sides it was almost purely fibrinous; the clot on the right side was larger than on the left; a fibrinous clot extended down the aorta."*

I do not know how the bibulous paper was arranged in the inhaler in this instance, nor whether the inhaler was used with a view to regulating the amount of vapour in the inspired air. The proportion of vapour must have been small during the first ten minutes, as the patient became so slowly insensible; and judging from the result, we must conclude that the proportion was large just before the accident. The firm coagulation of the blood and separation of the fibrin were probably owing to the galvanism which was so promptly applied. I found the fibrin separated from the colouring matter of the blood in the cavities of the heart of a cat, in which shocks of electro-magnetism had been sent through the chest just after it had been killed with chloroform.

* Medical Times and Gazette, 1854, vol. ii, p. 86.

(*To be continued*)

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